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ORIGINAL ARTICLE

Chest wall tumors: optimizing survival through prognostic factors and reconstruction

Salih Duman[1] · Eren Erdoğdu[1] · Arda Sarigül[1] · Berker Özkan[1] · Adalet Demïr[1] · Murat Kara[1] · S. Alper Toker[2]

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Abstract

Background Primary malignant chest wall tumors, originating from the bones, are infrequent neoplasms. Given its heterogeneity, further research is needed to understand the implications of recurrence and related factors in patients undergoing chest wall resection.

Aims We analyzed the association between the clinicopathological characteristics of these patients and their overall-survival (OS) and disease-free-survival (DFS).

Methods In this study, we conducted a retrospective analysis on patients who underwent chest wall resection for primary malignant bony chest wall tumors between 2000-2023.

Results Fifty-one patients were included. The presence of Ewing tumor, prior adjuvant therapy, postoperative complications, and reduced surgical margin were significantly associated with DFS and OS in both survival and univariate analyses. The optimal surgical margin threshold was identified as greater than 3 cm. Multivariate analysis revealed that only histopathological diagnosis of Ewing tumor and an insufficient margin remained significant for worse DFS and OS ($p = 0.041$ and 0.024, respectively). The 5-year overall survival (OS) and disease-free survival (DFS) rates were 53.6% and 50.8%, respectively.

Conclusion Ensuring effective surgery of chest wall tumors necessitates a surgical margin greater than 3 cm. Furthermore, the histopathologic classification of Ewing carcinoma emerges as another determinant impacting DFS and OS.

Keywords Thoracic wall · Ewing · Bone · Tumor · Surgery

Introduction

Chest wall tumors (CWT) can be categorized as either primary, metastatic, or originating from neighboring organs and infiltrating the adjacent chest wall. Primary malignant CWTs mostly manifest as mesenchymal neoplasms, and can arise from the bones, cartilages, and soft tissues of the chest wall [1, 2]. These neoplasms are considered rare, comprising less than 5% of all thoracic malignancies [2]. Approximately 55% of primary malignant CWTs originate from bones or cartilages, with the ribs being the most affected bones, followed by the scapula, sternum, and clavicle [3, 4]. Bony CWTs predominantly manifest as chondrosarcomas and osteosarcomas [4, 5]. Although it is uncommon in adults, Ewing sarcoma, originating from bones, is the most prevalent primary chest wall tumor in children and typically affects a single rib [6, 7].

Primary bony chest wall tumors (CWTs), encompassing a highly diverse patient population, necessitate individualized management strategies based on tumor diagnosis, location, and size. While a multidisciplinary approach consisting of surgery, chemotherapy, and radiotherapy is essential for treating malignant CWTs, achieving radical resection with wide margins of tumor-free tissue stands as the foremost determinant of extended survival [8]. Notably, patients who experience local recurrence or distant metastasis following surgical resection tend to exhibit shorter overall survival

✉ Arda Sarigül
sarigul.arda.md@gmail.com

[1] Department of Thoracic Surgery, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey

[2] Department of Cardiovascular and Thoracic Surgery, West Virginia University Heart and Vascular Institute, Morgantown, WV, US

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rates [9]. Due to the inherent heterogeneity of these tumors, prognostic factors for primary malignant CWTs in individuals undergoing chest wall resection are still under investigation. Therefore, the objective of this study is to assess the impact of recurrence and associated factors in patients with primary malignant bony chest wall tumors who have undergone chest wall resection.

Materials and methods

Clinical features

We conducted a retrospective analysis of patients who had undergone chest wall resection for primary malignant bony chest wall tumors between January 2008 and December 2023. We documented the clinical, radiological, and histopathological characteristics of these individuals. Those patients for whom follow-up data on recurrence or survival could not be obtained were excluded from the study.

All patients underwent a preoperative assessment that consisted of a physical examination, laboratory tests, chest computed tomography (CT), positron emission tomography/computed tomography (PET/CT), and pulmonary function tests. In selected patients, magnetic resonance imaging (MRI) of the chest was utilized to identify potential invasion of neighboring structures. Prior to surgery, a histopathological diagnosis was achieved through core needle biopsy. The patients were assessed by a multidisciplinary team both before and after the procedure, with consideration given to the need for neoadjuvant or adjuvant therapy. If neoadjuvant treatment was recommended, the surgical intervention was scheduled within a timeframe of 4–6 weeks after completion of the prescribed treatment.

We aimed to achieve a resection margin of 4 cm in all directions. However, in instances where important structures such as the spinal cord or vascular structures were involved, we endeavored to attain a minimum margin of 2 cm. The largest diameter of the defect was recorded. Therefore, R1 and R2 resections were excluded from the analysis due to their unexpected survival outcomes.

Extended resection was defined as a combined resection that encompassed multiple distinct structures. Each patient underwent preoperative and intraoperative assessments to determine the most suitable reconstruction method, considering oncological principles and the surgeon's preferences. Bone reconstruction primarily involved the utilization of titanium bars, methyl-methacrylate, propylene mesh, dual mesh, or a combination thereof. In terms of soft tissue reconstruction, pedicled flaps such as the latissimus dorsi, pectoralis major, and rectus abdominis were commonly employed.

Statistical analysis

In the statistical analysis, categorical variables were analyzed with the Chi-square and Fisher's exact tests as appropriate in contingency tables, whereas Student's t-test and Mann Whitney U-test were performed as appropriate for comparison of continuous variables. The logistic regression analysis was applied for univariate and multivariate analyses to confirm the impact of clinical and pathological factors on recurrence. Recurrence defined as local or distant relapse of the disease in any time after the surgery. Factors were included in multivariate tests if $p < 0.05$. Kaplan-Meier method was used to estimate the overall and recurrence-free survival. Data were expressed as mean ± the standard deviation. Any p value less than 0.05 was considered statistically significant. All statistical analyzes were performed with the Statistical Package for Social Sciences (SPSS, version 25.0, Chicago, IL, USA).

Results

We have total 51 patients with resected bony CWTs. The patient population consists of 33 (64.7%) males and 18 (35.3%) females with a mean age of 29.7 ± 13.8. Leading symptom was pain in 25 (49%) patients, followed by swelling in 19 (34.5%) patients, while 7 (13.7%) patients were asymptomatic. The mean size of the tumor in these patients is 59 ± 39 mm ranging from 12 to 220 mm. Based on recommendations from a multidisciplinary team upfront surgery was performed in 30 (58.8%) patients. Within neoadjuvant group 12(23.5%) patients received chemoradiotherapy, 6 (11.8%) patient chemotherapy (CT) and 3(5%) patient radiotherapy (RT) before surgery(Table 1).

Operative procedures

All patient, underwent conventional thoracotomy, while the Grünenwald incision was utilized for these specific cases. The average number of resected ribs was 3 ± 1.2. Twenty four patients, accounting for 47.1% of the total, underwent en-bloc, which involved the removal of ribs, lung, diaphragm, sternum, vertebrae, or various combinations thereof.

The average measurement of the largest defect's diameter was 122 ± 453 mm. Our approach to chest wall reconstruction involved the utilization of titanium bars in 15 cases (29.4%), a combination of methyl methacrylate and propylene mesh (sandwich graft) in 10 cases (19.6%), a combination of titanium bar and dual mesh methyl in 10 cases (19.6%), and the use of titanium bar with propylene graft in 4 case (7.8%). Chest wall reconstruction was deemed

Table 1 Clinicopathological features of the patients with bony chest wall tumor

	n (%)	Mean ± SD	Range
Age (mean ± SD)		29.7 ± 13.8	7–54
Gender			
Male	33 (64.7)		
Female	18 (35.3)		
Symptoms			
Pain	25 (49.0)		
Swelling	19 (37.3)		
Asymptomatic	7 (13.7)		
Side			
Left	29 (56.9)		
Right	22 (43.1)		
Tumor size (in mm)		59 ± 39	12–220
Histopathologic subtype			
Chondrosarcoma	26 (51.2)		
Ewing	21 (41.2)		
Osteosarcoma	4 (7.8)		
Neoadjuvant treatment			
CT	6 (11.8)		
RT	3 (5.9)		
CRT	12 (23.5)		
None	30 (58.8)		
Complication			
Absent	35 (68.6)		
Present	16 (31.4)		
Complication type			
Pneumonia	12 (23.5)		
Hemorrhage	1 (2)		
Graft infection	2 (3.9)		
Chylothorax	1 (2)		
Median Hospital Stay (in days)		7 ± 6.3	3–30
Adjuvant treatment			
CT	6 (11.8)		
RT	13 (25.5)		
CRT	9 (17.6)		
None	23 (45.1)		
Recurrence			
Absent	27 (52.9)		
Present	24 (47.1)		

SD, standard deviation; CT, chemotherapy; RT, radiotherapy; CRT, chemoradiotherapy

Table 2 Resection and reconstruction of bony chest wall tumors

	n (%)	Mean ± SD	Range
Resected rib count		3 ± 1.2	1–5
Simple Resections	**27 (52.9)**		
Extended resections	**24 (47.1)**		
Rib + Lung	11 (21.6)		
Rib + Diaphragm	4 (7.8)		
Rib + Vertebrae	3 (5.9)		
Rib + Diaphragm + Lung	2 (3.9)		
Rib + Clavicle + Sternum	2 (3.9)		
Rib + Lung + Sternum	1 (2)		
Rib + Lung + Vertebrae	1 (2)		
Defect Size (in mm)		122 ± 53	70–380
Margin (in mm)		30.8 ± 6.4	20–40
20 mm	6 (11.8)		
25 mm	10 (19.6)		
30 mm	14 (27.5)		
35 mm	11 (21.6)		
40 mm	10 (19.8)		
Chest wall reconstruction	**43 (84.3)**		
Titanium Bar + Dual Mesh	10 (19.6)		
Methyl methacrylate + propylene mesh (sandwich graft)	10 (19.6)		
Propylene Mesh	9 (17.6)		
Dual Mesh	7 (13.7)		
Titanium Bar + Propylene	4 (7.8)		
Polytetraflouroethylene(PTFE) graft	2 (3.9)		
Titanium Bar	1 (2)		
Soft tissue reconstruction			
pedicled latissimus dorsi flap	7 (13.7)		
pectoralis major flap	3 (5.9)		
rectus abdominis	1(2)		
pedicled latissimus dorsi flap + serratus anterior	1(2)		
Graft removal	**2 (6.8)**		
Graft infection	1 (3.4)		
Titanium graft skin abrasion and exposure	1 (3.4)		

unnecessary in 8 cases (15.6%). Soft tissue reconstruction entailed the implementation of pedicled latissimus dorsi flap in 7 cases (13.7%), pectoralis major flap in 3 cases (5.9%), and rectus abdominis in 1 case (2%) and one patient had combined pedicled latissimus dorsi flap plus serratus anterior flap (Table 2).

Postoperative follow-up

The median length of hospital stay was documented as 7 ± 6.3 days (3–30). Instances of complications were identified in a cumulative of 16 individuals, constituting 31.4% of the overall cases. Among these, nosocomial pneumonia emerged as the most prevalent complication, impacting 12 (23.5%) of the patients, whereas 1 (2%) necessitated blood transfusion due to massive bleeding, and 1(2%) encountered chylothorax. Two patients had graft removal due to graft infection 2(3.9%).

Among the patients, the prevailing histopathological subtype detected was identified as Ewing sarcoma in 21 cases, representing 41.2% of the overall sample. Chondrosarcoma is the most common subtype, found in 26 patients (51%), while osteosarcoma was documented in 4 individuals (7.8%) (Table 1).

Survival outcome and prognosis

Recurrence was detected in 24 patients, making up 47.1% of the total cohort. The rates of disease-free survival (DFS) at intervals of 1, 3, and 5 years stood at 76.4%, 53.3%, and 50.8% respectively, while the corresponding rates for overall survival (OS) were 86.3%, 66.8%, and 53.6%. No significant difference was observed in relation to age groups, gender, admission symptoms, tumor size and extended surgery in terms of DFS and OS. Histopathologic subtype and tumour margin impacted both DFS and OS ($p=0.001$). Neoadjuvant treatment was associated with improved DFS($p=0.008$) but did not demonstrate statistically benefit in OS($p=0.079$). However, survival analysis revealed that Ewing tumors exhibited the poorest DFS and OS ($p<0.01$, $p<0.01$), and the utilization of adjuvant treatment was also associated with unfavorable DFS and OS ($p=0.228$, $p=0.148$) respectively. Furthermore, complications were found to exert a substantial impact on DFS ($p<0.001$) but not associated with OS ($p=0.316$) (Table 3). Patients with a surgical margin of ≥3 cm demonstrated significantly longer mean survival compared to those with margins≤2 cm (175.8 vs. 83.4 months, $p=0.022$), indicating that wider resection margins are associated with improved overall survival (Fig. 1).

Histopathological subtype, neo- adjuvant treatment, and margin revealed significant impacts on DFS in the univariate analysis. Survival analysis revealed a significant difference among histopathological subtypes ($p=0.003$). Patients with chondrosarcoma exhibited the longest mean survival time (139.9 ± 12.4 months), followed by Ewing sarcoma (79.1 ± 20.6 months) and osteosarcoma (49.7 ± 17.8 months). However, upon further analysis using multivariate regression, it emerged that only margin ($p=0.068$) remained near-close the statistically significant (Table 4) (Figs. 2 and 3).

Table 3 Prognostic differences in subgroups of clinicopathological features in patients with bony chest wall tumor

Clinicopathological features	No. of patients (%)	5-year DFS (%)	*p*-value	5-year OS (%)	*p* value
Total	51	55		60.8	
Age	31 (51.7)	49.1	0.753	51.9	0.933
≤30	20 (48.3)	53.1		55.7	
>30					
Gender	18 (35.2)	66.7	0.139	64.8	0.259
Female	33 (64.7)	41.4		46.5	
Male					
Symptoms	44 (86.3)	51	0.942	51.2	0.524
Symptomatic	7 (13.7)	53.6		68.6	
Asymptomatic					
Tumor Size (in mm)	31 (60.7)	62.6	0.067	62.2	0.197
≤59	20 (39.2)	35		42.9	
>59					
Histopathological	21 (41.1)	20.8	**<0.001**	28.1	**0.001**
subtype	4 (7.8)	33		33	
Ewing	26 (50.9)	76.3		78.3	
Osteosarcoma					
Chondrosarcoma					
Histopathologic subtype	21 (41.2)	20.8	**<0.001**	28.1	**0.002**
Ewing sarcoma	30 (58.8)	72.1		73.6	
Others					
Neoadjuvant treatment	21 (41.2)	32.7	**0.008**	39.4	0.079
Yes	30 (58.8)	64.3		64.9	
No					
Adjuvant treatment	28 (54.9)	43.8	0.228	43.9	0.148
Yes	23 (45.1)	59		64.7	
No					
Extended surgery	24 (47.1)	39.4	0.147	44	0.316
Yes	27 (52.9)	61.7		63	
No					
Complication	16 (31.4)	34.4	**<0.001**	46	0.316
Yes	35 (68.6)	58.6		57.2	
No					
Tumor Margin (in mm)	6 (11.8)	0	**<0.001**	20	**0.001**
<25	10 (19.5)	20		20	
25<30	14(27.5)	71		71.4	
30<35	21 (41.2)	67.4		76.9	
>35					

OS, overall survival. DFS, disease free survival

Discussion

Tumors originating from bony or cartilaginous tissues in the chest wall are uncommon neoplasms. Due to their highly diverse nature, these tumors require individualized management through a multidisciplinary approach that encompasses surgical intervention [2]. Prognostic factors that affect overall or disease-free survival (OS or DFS) in patients who undergo surgery with the diagnosis of bony chest wall tumor are still being investigated. In this study, we retrospectively analyzed the clinical and histopathological features affecting OS and DFS in 51 patients who underwent chest wall resection with the diagnosis of primary malignant bony chest wall tumor. The Ewing sarcoma subtype, the use of additional treatment methods, the adequacy of surgical margin, and the occurrence of complications were found to be considerable factors impacting both overall survival OS and DFS in the univariate analyses. Nevertheless, in the multivariate analysis, only Ewing carcinoma and margin emerged as statistically significant parameters.

Only a limited number of research studies have explored primary chest wall tumors originating from bony or cartilaginous tissues. Various studies on soft tissue sarcomas have indicated that a higher tumor grade is linked to inferior overall and disease-free survival outcomes [10–15]. The impact of tumor grade on both the progression free survival (PFS) and the development of distant metastases in primary

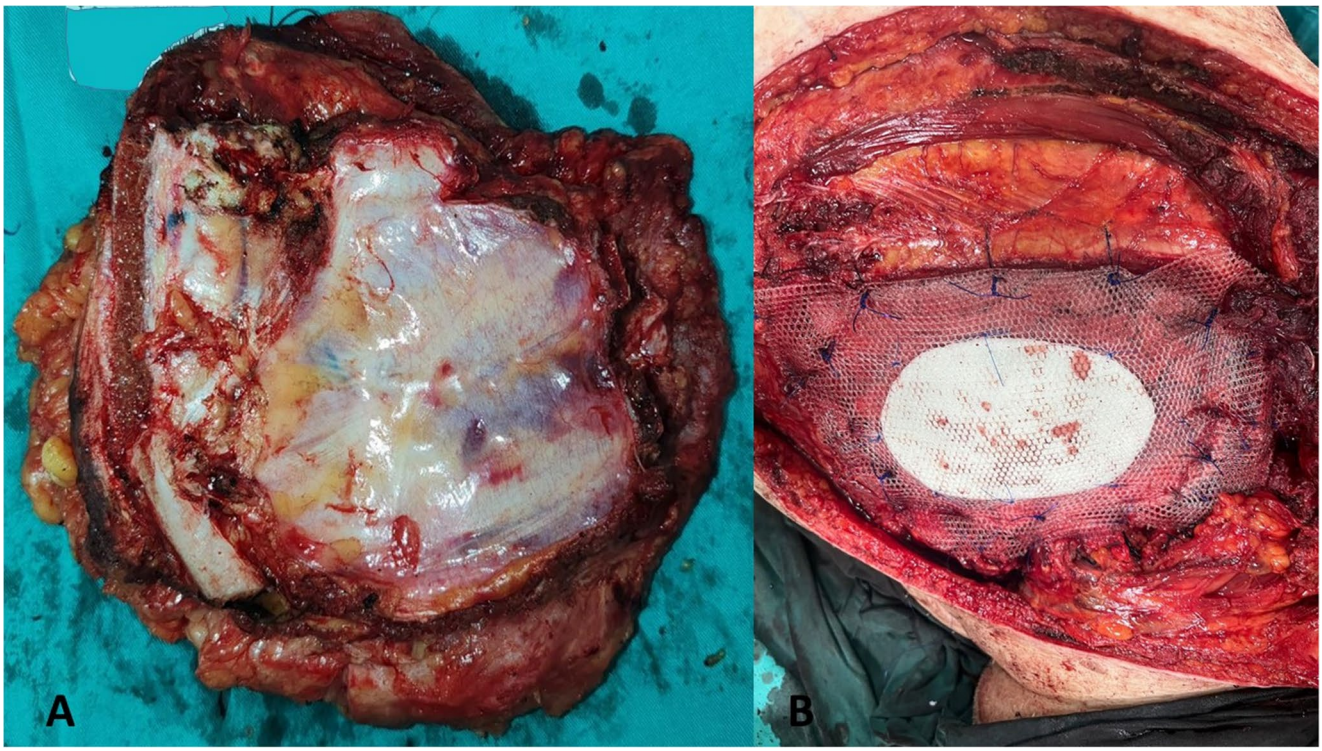


Fig. 1 Chest wall sarcoma resected (**A**) and reconstructed with reconstruction materials (**B**)

Table 4 Univariate and analysis of the prognostic factors by Cox Proportional-Hazards regression model

	Disease-free survival			Overall Survival		
Variable	Relative Risk	95% Confidence Interval	p Value	Relative risk	95% Confidence Interval	p Value
Univariate						
Neoadjuvant Therapy (Present vs. Absent)	0.394	(0.175, 0.886)	**0.02**	1.646	(0.678, 3.994)	0.271
Histopathological Subtype (Ewing vs. other)	0.215	(0.091, 0.507)	**<0.01**	1.590	(0.643, 3.933)	0.315
Margin (<30 vs.≥30 mm)	0.19	(0.082, 0.436)	**<0.01**	0.897	(0.243, 3.309)	0.869
MULTIVARIATE						
Neoadjuvant Therapy (Present vs. Absent)	0.781	(0.420, 1.452)	0.44	1.344	(0.420, 1.452)	0.435
Histopathological Subtype (Ewing vs. other)	0.184	(0.020, 1.701)	0.14	0.569	(0.020, 1.701)	0.136
Margin (<30 vs.≥30 mm)	0.322	(0.095, 1.089)	0.07	1.692	(0.095, 1.089)	0.068

chondrosarcoma of the chest wall was also identified [16, 17]. The findings of Martini N. et al.'s study on surgical removal of primary sternal tumors have been published, indicating a correlation between tumor grade and histopathological subtype with the overall survival rate following a successful resection [18]. Our results demonstrating Ewing sarcoma subtype as a high-grade tumor is associated with poor DFS are consistent with former evidence. The evidence from our study aligns with previous findings, indicating that the Ewing sarcoma subtype, characterized by a high-grade tumor, is strongly correlated with unfavorable outcomes in terms of disease-free survival (DFS) and overall survival (OS).

Collaud S. et al. have concluded that extended resection beyond the chest wall and including intrathoracic structures is associated with poor progression free survival [19]. In our study nearly half of patients have undergone extended resections. We believe that the separation from the literature arises from differences in study design. Our study included a larger patient cohort and incorporated more cases of Ewing

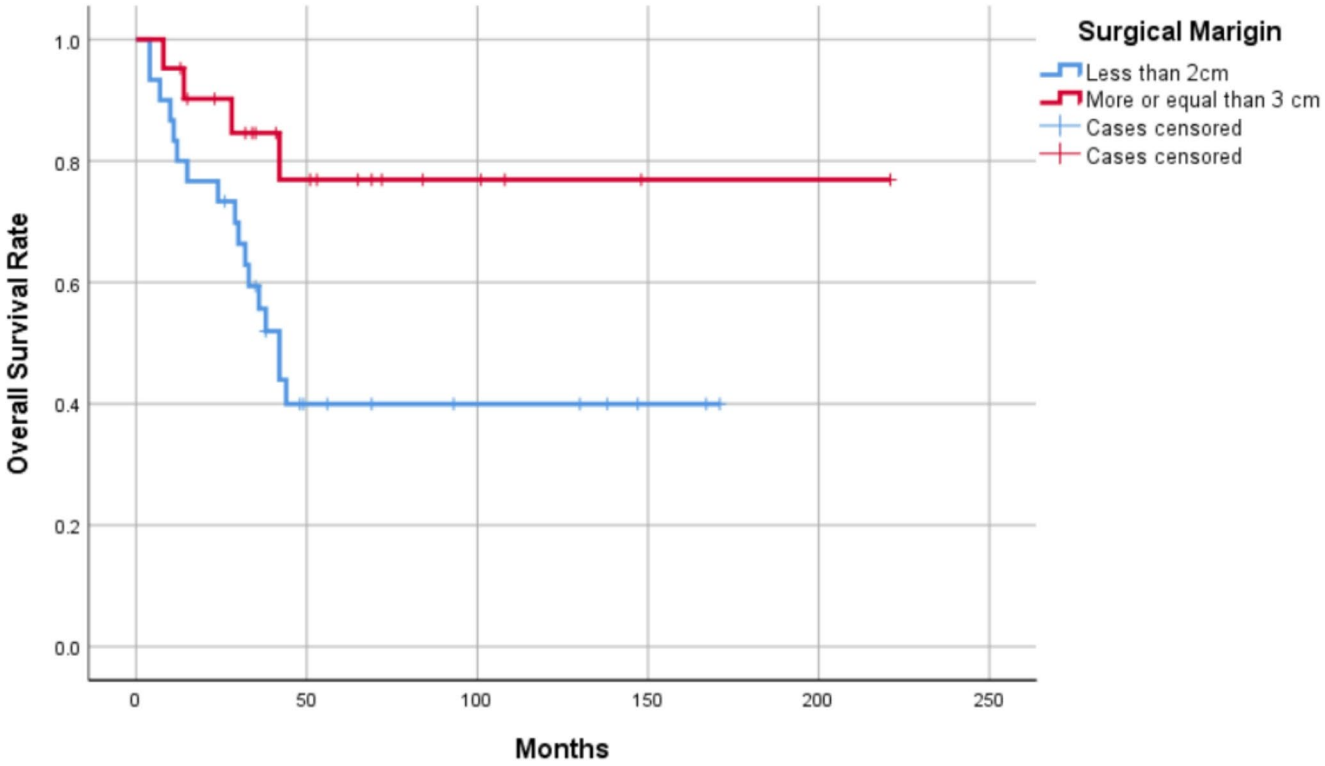


Fig. 2 Overall Survival by Surgical Marigin

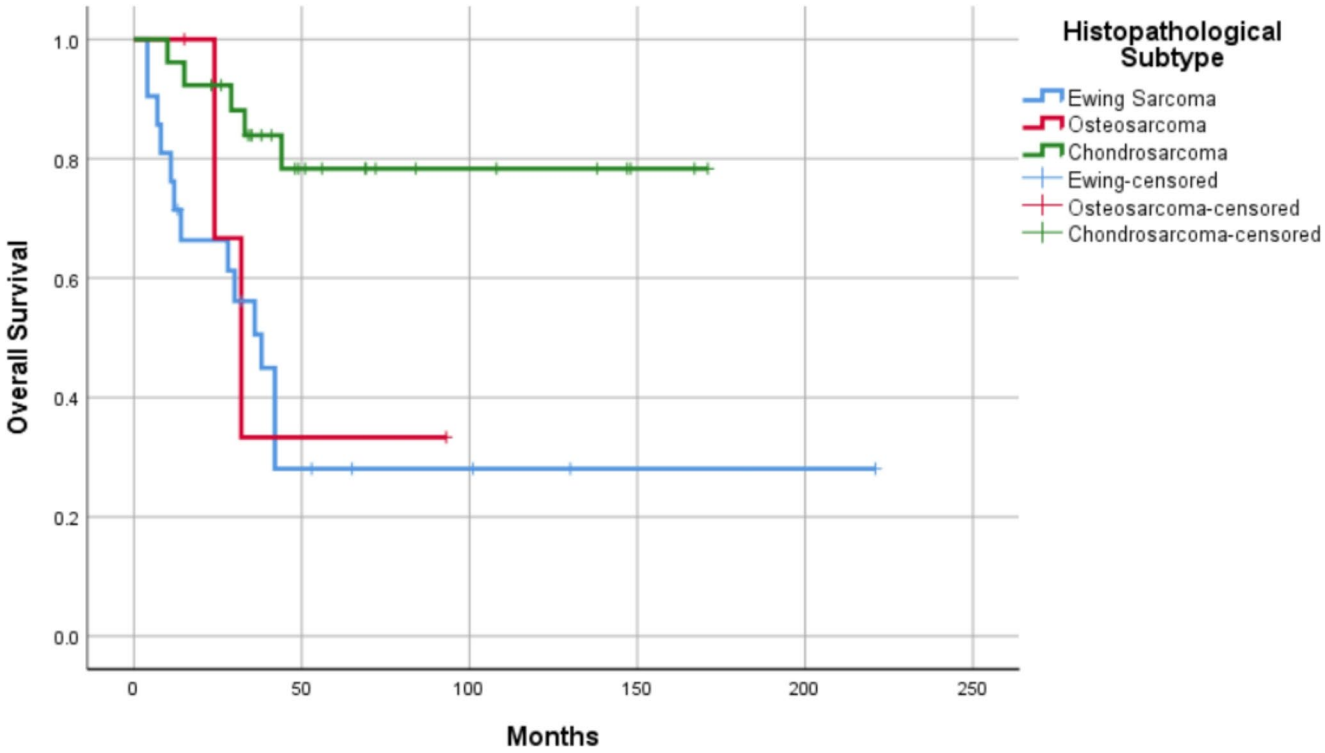


Fig. 3 Overall Survival by Histopathological Subtype

sarcoma. As a result, we found that extended resections were not associated with Overall Survival (OS) or Disease-Free Survival (DFS), in contrast to their findings. Furthermore, in a retrospective study in which primary chest wall Ewing sarcoma patients included, tumor volume more than 200 ml was found to have adverse effect on survival [20]. These conclusions may support our findings about worse effect of distant metastases and larger tumors on OS, related to high tumor burden or aggressiveness of the disease. In our study, we observed no association between the patient's survival and the size of the tumor.

Tumor free surgical margin is well-known prognostic factor for all chest wall tumors. R1 and R2 resection are associated with worst DFS and OS. However surgical margin which should be achived is still debated. Wang et al. published an expert consensus on this topic. A majority of the surgeons (51.2%) held the view that a margin distance of 2–3 cm should be ensured during the wide excision procedure. In addition, a notable proportion (20.2%) of surgeons believed that a margin distance of 3–4 cm should be guaranteed, whereas a smaller percentage (13.1%) advocated for obtaining a margin distance of 4–5 cm. In accordance with the expert consensus published by Wang et al. (2021), most thoracic surgeons recommend a 2–3 cm margin during wide excision, while some advocate for 3–4 cm to ensure oncological safety. Our findings corroborate this consensus, identifying 3 cm as a critical margin threshold beyond which DFS and OS outcomes significantly improve ($p=0.041$ and $p=0.024$, respectively). These results reinforce the practical importance of defining an adequate resection distance in optimizing survival [21]. In alignment with literature, our study identifies a surgical margin greater than 3 cm as a key threshold, below which DFS and OS outcomes significantly deteriorate ($p=0.041$ and 0.024, respectively). This threshold aligns with established surgical principles; however, our results add clarity by demonstrating that once this margin is achieved, other prognostic factors most notably as histopathological subtype could pronounce role in survival outcomes.

Foroulis et al. reported an overall complication rate of 27%, primarily highlighting wound infections and pneumonia, while Martini et al. observed a similar rate of 30%, emphasizing wound infections and respiratory complications. In comparison, our study reported a slightly higher overall complication rate of 31.4%, with nosocomial pneumonia (23.5%) being the most common issue, followed by hemorrhage (2%) and graft removal due to infection (3.9%). Because the existing literature is limited by small patient populations, there are no data on graft removal after surgery [8, 18].

Adjuvant treatment following wide surgical resection is controversial in primary chest wall tumors [4]. While chemotherapy has a role in the neoadjuvant setting for osteosarcoma and Ewing sarcoma, radiotherapy is recommended to be reserved for positive margins after surgical resection [21]. We found that the patients who had adjuvant treatment had shorter DFS and OS in the current study. Nakahashi N. et al. have also demonstrated that adjuvant chemotherapy has an adverse effect on 5-year DFS rate (20% vs. 41%, $p=0.04$) in patients with primary chest wall soft tissue sarcomas [22]. These findings may be explained with the insufficient benefit of chemotherapy and radiotherapy compared to its adverse effects on disease-free course.

The present investigation is constrained by several factors. The scarcity and variety of primary bony chest wall tumors restrict the number of patients available for analysis. Moreover, the retrospective design of the study which covers an 18-years period, may have impacted the results. Additionally, the integration of a multidisciplinary approach incorporating preoperative assessments, surgical planning, and reconstruction strategies reflects real-world clinical practices, improving the study's translational relevance. Lastly, the detailed evaluation of reconstruction techniques, including the use of titanium bars, sandwich grafts, and pedicled flaps, provides technical insights that are valuable for optimizing postoperative outcomes.

Conclusion

In patients diagnosed with primary bony chest wall tumors the presence of the Ewing sarcoma subtype poses a significant unfavorable prognostic impact on both OS and DFS. It is highly recommended to aim for a surgical margin exceeding 3 cm. These findings highlight the necessity of a multidisciplinary and personalized treatment strategy, emphasizing both the critical nature of achieving adequate surgical margins and the potential for tumor-specific factors, such as histopathological subtype, to further guide therapeutic decision-making. Further investigation is required to explore the various factors that influence overall survival.

Author contributions S.D., A.S. and E.E. helped the conceptualization and study design.
E.E., A.S. and A.D. collected the data and helped extensive literature research.
M.K. and S.D. analyzed the data.
S.D., E.E and B.O. helped the manuscript writing.
A.T. and A.D. helped repeated editing and reviewing the manuscript.

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Declarations

Ethical approval This retrospective study was approved by ethics committee of our university by the number 2023/705.

Ethical standards Our study has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all patients for their anonymized information to be stored in the hospital database and used for clinical research as well as to be published in this article.

Conflict of interest The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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