

## Original Article

## Parosteal Osteosarcoma: Radiologic and Prognostic Features

## Parosteal Osteosarkom: Radyolojik ve Prognostik Özellikler

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## ABSTRACT

**Aim:** The aim of this study is to evaluate significance of Magnetic Resonance Imaging (MRI) characteristics and their effects on surgical margins, prognosis, oncological and functional outcomes of parosteal osteosarcoma in our clinic.

**Patients and method:** Fifteen patients (4 male/11 female) who operated with the diagnosis of parosteal osteosarcoma in our clinic were retrospectively reviewed. The epidemiological data, biopsy method and delay in diagnosis are noted. The lesions maximum circumferential extension, intramedullary involvement and neurovascular extension in MRI sections were evaluated. The resection type (segmental articular/hemicortical) and surgical margins were noted. Functional and oncological results at last follow-up were assessed.

**Results:** The mean age was 31.7 (17-71) years; mean follow-up was 50.1 (24-176) months. The most common site was distal femur. The closed biopsies were related with increased number of re-biopsies and misdiagnosis/improper interventions. ( $p<0.001, p=0.023$ ) Intramedullary involvement percentage was related with maximum circumferential extension percentage ( $p=0.006$ ) The intramedullary involvement ratio of  $\leq 25\%$  suggested no recurrence or metastasis. The mean MSTS score was 87.8% (range, 60-100%). The neurovascular involvement was related with metastatic disease, deep infections and complication related surgeries. ( $p=0.017, p=0.002, p=0.005$ ) The most common resection type was segmental articular resection (9 patients). Hemicortical resections with biological reconstructions had the best MSTS scores. ( $p=0.002$ ) The maximum circumferential extension percentage, intramedullary involvement percentage and neurovascular involvement showed lower MSTS scores. The 5-year overall survival was 92.3%, local recurrence-free survival was 86.2% and metastasis-free survival was 86.2%.

**Conclusion:** The reliability of needle biopsy sampling is controversial in parosteal osteosarcomas. The lesions extent of intramedullary involvement, neurovascular bundle proximity and maximum periosteal circumferential extension on MRI should be considered when planning the surgery. The evaluation of maximum circumferential extension on MRI is crucial for the resection margins.

**Keywords:** Parosteal Osteosarcoma, Radiological evaluation, Prognostic criteria, Biopsy method, Tumor endoprosthesis

## ÖZET

**Giriş ve Amaç:** Parosteal osteosarkomlar nadir gözlenen bir osteosarkom tipidir. Klasik olarak kemoterapi ve radyoterapiye duyarsız, düşük dereceli bir lezyondur. Ancak kolaylıkla çevre dokulara invazyon gösterebilmektedirler. Amacımız parosteal osteosarkomlarda manyetik rezonans görüntüleme (MRG) ile tespit edilen özelliklerin; cerrahi sınır, prognoz, onkolojik ve fonksiyonel sonuçlara etkilerini değerlendirmektir.

**Yöntem ve Gereçler:** Kliniğimizde 2006-2018 yılları arasında parosteal osteosarkom tanısı ile cerrahi tedavi uygulanmış asgari 2 yıl takip edilmiş 15 hastanın (4 Erkek/11 Kadın) klinik ve radyolojik verileri retrospektif olarak değerlendirildi. Epidemiyolojik verilerin yanında tanı için uygulanan biyopsi yöntemi (açık/kapalı) ve tanıda gecikme süresi not edildi. Hastaların tanısız MRG kesitlerinde lezyonun azami çevresel uzanım oranı, intrameduller tutulum oranı ve nörovasküler paket tutulumu

değerlendirildi. Rezeksiyon tipleri (segmental ekleme uzanan/hemikortikal) ve rezeksiyon sonrası cerrahi sınırlar değerlendirildi. Hastaların son kontrollerindeki fonksiyonel ve onkolojik sonuçları değerlendirildi.

**Bulgular:** Çalışma grubumuzda ortalama yaş 31.7(17-71), ortalama takip süresi 50.1(24-176) ay idi. En sık tespit edilen tutulum distal femurdu. Kapalı biyopsi yöntemlerinin tekrarlayan biyopsiler/yanlış tanı/uygunsuz girişimlere yol açtığı belirlendi( $p<0.001$ ,  $p=0.023$ ). Lezyonun intramedüller tutulum oranının, azami çevresel uzanım miktarı ile ilişkili olduğu belirlendi( $p=0.006$ ). %25'in altında intramedüller tutulum oranının yapılan uygun rezeksiyonlarla nüks veya metastazlara yol açmadığı belirlendi. Ortalama MSTS skoru %87.8 idi. Nörovasküler tutulum varlığının metastazlar, derin enfeksiyonlar ve tekrarlayan cerrahiler ile ilişkili olduğu belirlendi ( $p=0.017$ ,  $p=0.002$ ,  $p=0.005$ ). En sık uygulanan rezeksiyon tipi segmental, ekleme uzanan rezeksiyon (9 hasta) idi. Hemikortikal rezeksiyon ve biyolojik rekonstrüksiyonların en iyi MSTS skorlarına sahip olduğu belirlendi ( $p=0.002$ ). Yüksek azami çevresel uzanım miktarı, intramedüller tutulum oranı ve nörovasküler tutulum varlığının düşük MSTS skorları ile ilişkili olduğu belirlendi. 5-yıllık genel sağkalımın %92.3, lokal-progresyonsuz sağkalımın %86.2 ve metastassız sağkalımın ise %86.2 olarak tespit edildi.

**Tartışma ve Sonuç:** Parosteal osteosarkomlarda iğne biyopsisinin güvenilirliği sorgulamaya açıktır. Tanısal MRG'de ekleme uzanım kadar lezyonun azami çevresel uzanım miktarı, intramedüller tutulum oranı ve nörovasküler tutulum varlığı cerrahi öncesi planlamada ve rekonstrüksiyon yöntemi belirlemede önem taşımaktadır. MRG'de lezyonun azami çevresel uzanım miktarı cerrahi sınırları belirleyebilmek açısından önem taşımaktadır.

**Anahtar Kelimeler:** Parosteal osteosarkom, Radyolojik değerlendirme, Prognostik kriterler, Biyopsi yöntemi

## Introduction

Parosteal osteosarcoma is a rare surface osteosarcoma variant which commonly involves the metaphyseal ends of the bones [1-4]. The well-differentiated, insidious character of the tumor may lead to delayed diagnoses and symptoms [1,3-6]. Wide resection is the recommended treatment regarding its low-grade malignant potential and low potential to metastasize [4,6,7]. Although parosteal osteosarcoma are mostly encountered as low grade, intermediate and dedifferentiated high grade types are not rare [4,6-9]. Low and intermediate grade variants mostly show better survival however dedifferentiated high grade variants have worse outcomes by means of both local progression and metastasis [4,7]. The incidence of local recurrences in parosteal osteosarcoma mostly depends on the quality of surgical margins and can even be detected within twenty years postoperatively [3,4,6-10].

The lesions in close proximity to the neurovascular structures is a major problem

particularly as a result of recurrent biopsies or operations [3]. The other most common pitfall encountered in parosteal osteosarcoma patients is being misdiagnosed and improperly intervened as benign lesions [3-6]. There is also a debate in determining the treatment method and prediction of local recurrence in detection of intramedullary extension on magnetic resonance imaging (MRI) [2,3,11,12]. A meticulous pre-operative planning by MRI is recommended to define resection margins and histologic grade [11,13].

In our study we sought to evaluate significance of MRI findings and surgical margins on prognosis with oncological and functional outcomes by the retrospective single center experience of parosteal osteosarcoma.

## Patients and Method:

The clinical and radiological data of 23 patients who received surgical treatment with

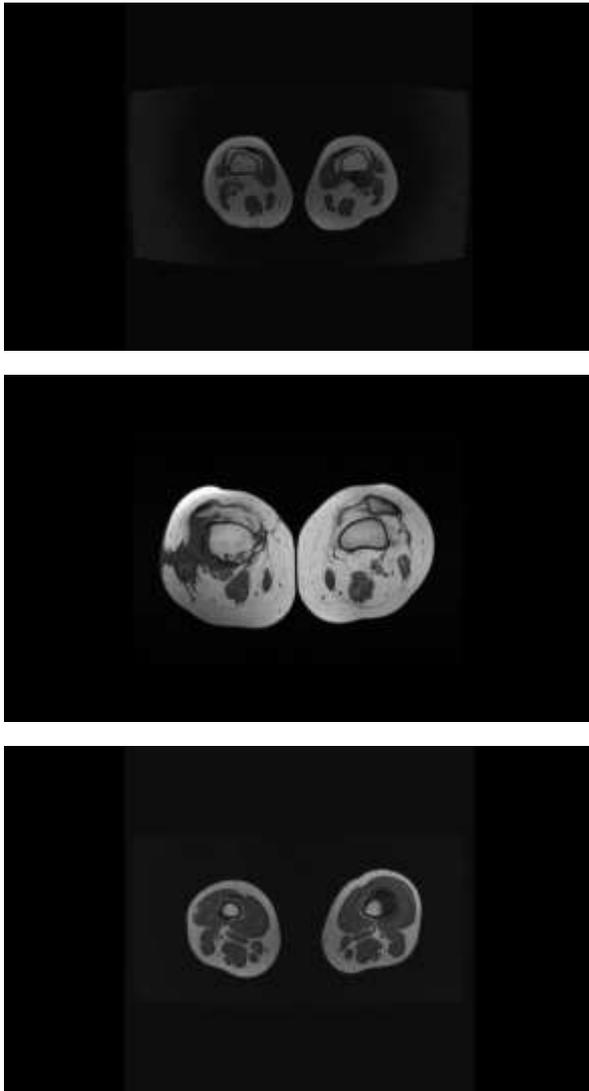


Figure 1. The examples of circumferential extension of the cases in our study. T1 weighted contrast enhanced series of the patients are evaluated and approximately (A) 30% circumferential extension, (B) 50% circumferential extension and (C) 75% circumferential extension of the parosteal osteosarcoma examples are demonstrated.

the diagnosis of parosteal osteosarcoma in our institution between May 2006 and February 2018 were retrospectively reviewed. Five patients had limited radiological data, two patients had their parosteal osteosarcoma diagnosis and management in elsewhere center and a patient was lost to follow-up. Thus, eight patients were excluded and 15 patients (4 male/11 female) were included in the study group.

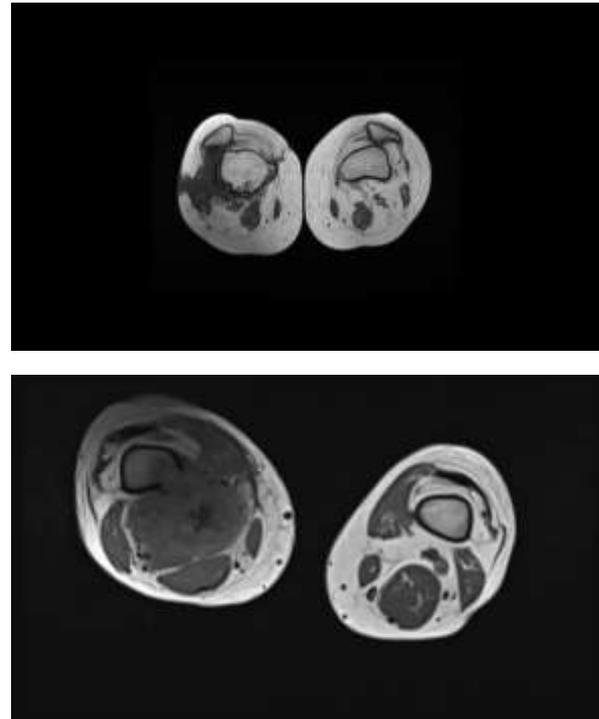


Figure 2: The examples of intramedullary involvement percent of the cases in our study. T1 weighted contrast enhanced series of the patients are evaluated and approximately (A) <10% intramedullary involvement, (B) 75% intramedullary involvement examples from series are shown.

This study (no. 280) was assessed by Institutional Review Board of Baltalimanı Bone Diseases Training and Research Hospital in the 68th board meeting held in 02.03.2021. The board approved the research on compliance with the rules of ethics and scientific guidelines.

The epidemiological data was evaluated regarding site of the lesion and biopsy method. The histopathological diagnosis of longer than 3 months is accepted as delay in diagnosis. The delay in diagnosis and Enneking stage of the lesion were also noted.

Preoperative MRI assessment was performed regarding the lesion's maximum circumferential extension percentage in transverse sections (Figure 1). Intramedullary involvement was evaluated in T2 sections and

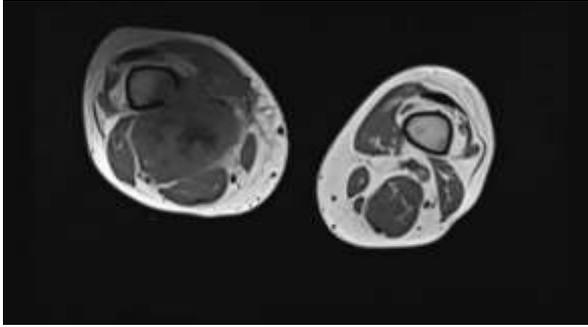


Figure 3: The examples of neurovascular involvement types in our series. T1 weighted contrast enhanced series demonstrate involvement of the neurovascular structures by the tumor.

contrast enhanced MRI series and the percentage of the involvement was noted (Figure 2). The neurovascular bundle involvements were also evaluated. (Figure 3) The patients are further evaluated regarding resection type (segmental intraarticular/hemicortical), histopathological margins. The occurrence of complications (infections, local recurrences, implant failures) during follow-up were noted. The MSTS scores of the patients at latest follow-up were also evaluated. The oncologic status at the latest follow-up was noted (continuous disease-free (CDF), no evidence of disease (NED), alive with disease (AWD) and died of disease (DOD)). The overall survival was defined as the interval in months, from the time of definitive surgical treatment to the last follow-up visit or death.

Recurrence-free survival and metastasis-free survival were defined as the interval in months with no evidence of local disease and metastatic disease after definitive surgical treatment, respectively. The statistical analysis of the observed values was performed using Fischer's exact test or Kruskal-Wallis test. The survival of the patients was evaluated by the Kaplan–Meier method with a log rank test. The independent factors effecting survivals were identified by cox regression analysis. Statistical analyses were performed

by using SPSS version 20.0 (SPSS, Chicago, IL). A p-value of  $< 0.05$  was considered statistically significant

### Results:

A total of 15 patients were included in the study group. The mean age was 31.7 years (median, 30; range, 17-71), mean follow up was 50.1 months, median follow-up was 30 (range, 24-176) months. The most common site was distal femur in 13 patients. Ten patients had previous biopsies in elsewhere centers. Our series suggested that previous core needle biopsies in elsewhere center was significantly related with the increased number of re-biopsies and misdiagnoses and/or improper interventions. ( $p < 0.001$ ,  $p = 0.021$ ) There was delay in diagnosis in 7 patients. Closed biopsy methods were significantly related with delayed diagnosis. ( $p = 0.044$ ) Nine patients were staged as Enneking IB, five patients were IIB and a patient with lung metastasis was staged as III. (Table 1) The maximum circumferential extension percentage was a crucial indication for selection of resection method in our series. The mean circumferential extension percentage was 39.0% in hemicortical resections whereas 47.8% in intraarticular resections. (Table 2) Intramedullary involvement was evident in 8 patients. Intramedullary involvement ratio was significantly correlated with the maximum circumferential extension percentage ( $p = 0.006$ ) The intramedullary involvement ratio of  $\leq 25\%$  suggested no recurrence or metastasis. Metastasis was related with intramedullary involvement ratio. ( $p = 0.004$ ) The neurovascular bundle proximity ( $< 5$  mm) or involvement was detected in 4 patients. Neurovascular involvement was significantly related with maximum circumferential extension percentage and intramedullary involvement percentage ( $p = 0.032$ ,  $p = 0.041$ ). Besides the presence of neurovascular

Table 1: Epidemiological data of the parosteal osteosarcoma patients in our series.

Variable	Value	
Mean age	31.7 (Range: 17-71, Median: 30)	
Gender	4 Male, 11 Female	
Localization	Distal Femur	13
	Proximal Tibia	1
	Distal Tibia	1
Biopsy method	Open Biopsy	9
	Needle Biopsy	6
Previous Biopsies	None	6
	Needle Biopsy	9
Misdiagnosis/Improper intervention	7	
Delay in diagnosis	>6 months	3
	3-6 months	4
Lung Metastasis	Diagnosis	1
	Follow-up	1
Enneking stage	IB	9
	IIB	5
	III	1

involvement was found to significantly related with metastatic disease, complication related surgeries and lower MSTS ( $p=0.017, p=0.005, p=0.026$ ).

The most common resection type was segmental articular resection in 9 patients. (Table 3) Histopathologically evaluated surgical margins were all tumor free. Prosthetic reconstructions were applied in nine patients, biologic reconstruction (liquid nitrogen recycled bone and hemicortical fixation) was performed in six. (Figure 4)

The parosteal osteosarcoma should meet two radiological criteria in preoperative MRI evaluation for consideration of hemicortical resections. Hemicortical resections with biological reconstructions demonstrated the best MSTS scores. ( $p=0.002$ ) (Figure 4) The maximum circumferential extension ratio, intramedullary involvement ratio and neurovascular involvement were inversely correlated with MSTS scores. ( $p=0.003, p=0.044, p=0.025$ ) In two patients vascular resections required reconstructions.

Table 2: The localization and preoperative radiological evaluation criteria of the patients in our series.

Patient No.	Localization	Maximum Circumferential Extension (%)	Intramedullary Involvement (%)	Neurovascular Bundle Involvement
1	Distal Femur	20	65	N/A
2	Distal Femur	40	75	Involvement
3	Distal Femur	80	<25	N/A
4	Distal Femur	40	<25	N/A
5	Distal Femur	25	<25	N/A
6	Distal Femur Proximal	40	<25	N/A
7	Tibia	75	<25	N/A
8	Distal Femur	50	80	Close Proximity (<5 mm)
9	Distal Femur	50	<25	N/A
10	Distal Tibia	50	100	Close Proximity (<5 mm)
11	Distal Femur	30	<25	N/A
12	Distal Femur	10	50	Involvement
13	Distal Femur	60	<25	N/A
14	Distal Femur	60	<25	N/A
15	Distal Femur	40	<25	N/A

The postoperative deep infections were encountered in two patients, local recurrences in two and distant metastases in two patients. Regarding the oncological status 15 patients were CDF and NED. The mean MSTS score was 87.8% (range, 60-100%). (Table 3)

The 5-year overall survival was 92.3%. (Figure 5) 5-year local recurrence-free survival was 86.2%. (Figure 6) 5-year metastasis-free survival was 86.2%. (Figure 7)

## Discussion

The low grade and well-differentiated character of parosteal osteosarcoma may lead to delayed symptoms and/or misdiagnoses [1,3-6]. Also repetitive biopsies or improper interventions with misdiagnosis may result in adhesions and local seeding of this malignancy [3-6]. As popliteal region is commonly involved, the lesion is mostly in close proximity to major popliteal neurovascular structures, which may also

complicated by repetitive procedures [3]. Regarding its low-grade character, limited local extension and low potential to metastasize, wide resection is recommended as the mainstay of treatment [4,6,7]. Determination of the treatment method and prediction of local recurrence in presence of intramedullary extension on magnetic resonance imaging (MRI) is debated [2,3,11,12]. We sought to evaluate the MRI findings, common diagnostic problems and their effects on prognosis with oncological and functional outcome differences in parosteal osteosarcoma.

We have found that seven of the fifteen patients in our study had more than one biopsy to achieve the definitive diagnosis and five of them was needle biopsy. The frequency of previous biopsies/delayed diagnosis ratio was higher in needle biopsy group. (p<0.001). The reliability of needle biopsies reported to be limited in determining not only the diagnosis but also the degree of anaplasia in parosteal



Figure 4: (A) Pre- and post-operative 1st year anteroposterior and lateral x-ray views of a 40-year-old patient who was applied segmental extraarticular resection and tumor endoprosthetic reconstruction. (B) Pre- and post-operative 2nd year lateral x-ray views of a 37-year-old patient who was applied hemicortical resection followed by fixation with screws is demonstrated.

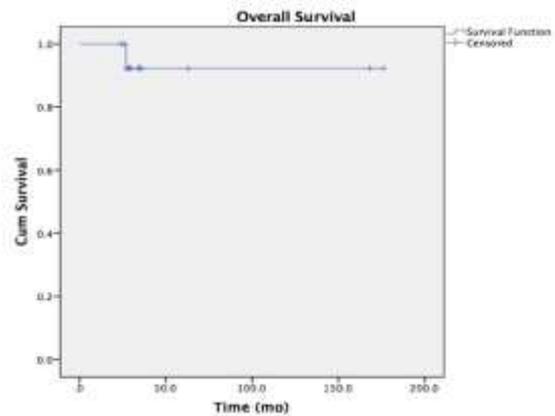


Figure 5: The Kaplan Meier survival curve demonstrating the overall survival of parosteal osteosarcoma in our series.

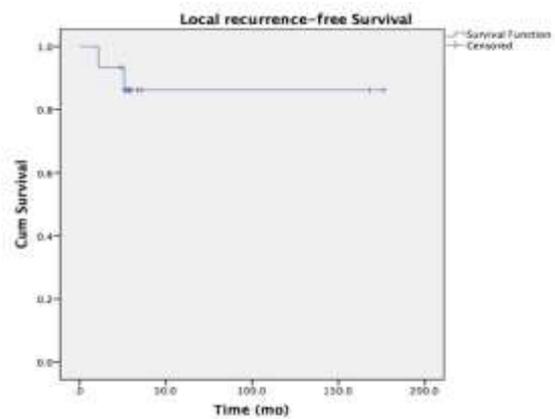


Figure 6: The Kaplan Meier survival curve demonstrating the local recurrence-free survival of parosteal osteosarcoma in our series.

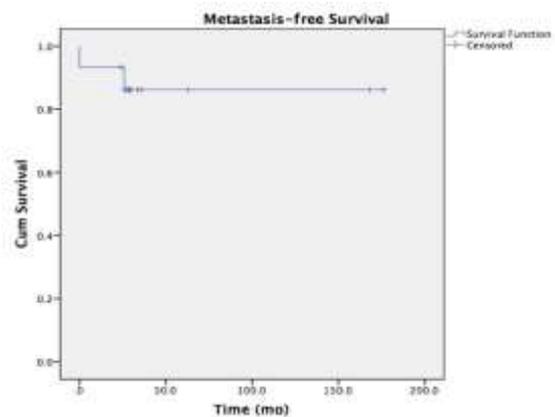


Figure 7: The Kaplan Meier survival curve demonstrating the metastasis-free survival of parosteal osteosarcoma in our series.

Table 3: The resection, reconstruction and surgical margin features with the outcome data of the patients in our series.

Patient No.	Resection Type	Surgical Margin	Reconstruction Type	Follow-up Time (mo)	Oncological Status	Local Recurrence (mo)	Metastasis (mo)	Deep Infection (mo)	MSTS Score (%)
1	Segmental	Negative	Tumor Endoprosthesis	36	NED	N/A	N/A	N/A	90
2	Segmental	Negative	Tumor Endoprosthesis	29	NED	N/A	N/A	4	87
3	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	34	NED	N/A	N/A	N/A	100
4	Segmental	Negative	Tumor Endoprosthesis	29	NED	N/A	N/A	17	90
5	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	168	CDF	N/A	N/A	N/A	100
6	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	34	NED	N/A	N/A	N/A	100
7	Segmental	Negative	Tumor Endoprosthesis	30	NED	N/A	N/A	N/A	93
8	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	176	CDF	N/A	N/A	N/A	100
9	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	27	NED	N/A	N/A	N/A	100
10	Segmental	Negative	Tumor Endoprosthesis	35	NED	26	26	N/A	70
11	Hemicortical	Negative	Liquid Nitrogen and Screw fixation	28	NED	N/A	N/A	N/A	80
12	Segmental	Negative	Tumor Endoprosthesis	27	DOD	N/A	0	N/A	60
13	Segmental	Negative	Tumor Endoprosthesis	26	NED	N/A	N/A	N/A	76
14	Segmental	Negative	Tumor Endoprosthesis	63	NED	11	N/A	N/A	83
15	Segmental	Negative	Tumor Endoprosthesis	24	NED	N/A	N/A	N/A	87

osteosarcoma [14]. Some authors reported a high rate of histological difference after total excision, which 60% of the needle biopsy revealed accuracy in final degree of the lesion, whereas this rate was 88% in open biopsy in the same study [4]. Previous biopsies and improper interventions constitute a major problem in achieving diagnosis and planning the treatment of parosteal osteosarcoma [4,14]. Each intervention on parosteal osteosarcoma, particularly in the popliteal region, requires extensive dissection of the surrounding soft tissues and neurovascular structures, which may cause adhesions [12]. These adhesions and scar tissue may complicate the diagnostic evaluation thus a detailed information on previous interventions is essential. One patient in our series had 4 closed biopsies in 5 years in elsewhere center however final diagnosis was achieved at 5th biopsy (open) in our clinic. Deep infections and complication related surgeries were thought to be related with repetitive interventions in our series.

The intramedullary changes were one of the major factors that helped the decision of resection type in our study. We assume that some intramedullary changes might be originated from the increased pressure inside the medulla, also we have detected limited intramedullary involvements around the vascular entry or tendinous/ligamentous attachment sites to the bone. The hemicortical resections including limited intramedullary involvement may be a method of choice. Bertoni et al. compared the radiologic and histopathologic findings of 18 parosteal osteosarcoma with intralesional radiolucencies and concluded that most of the high-grade components were located in deep radiolucency areas [12]. Han et al. have reported that in radiological evaluation (MRI, CT) 81% of their cases demonstrated intramedullary changes, however only 48% confirmed this radiological change [15]. They

have concluded that the disparity may be related to the exaggerated views on MRI [15]. Jelinek et al. had direct anatomic mapping and correlation in four high-grade parosteal osteosarcoma and concluded that three lesions demonstrated intramedullary extension by a low-grade component and only one high-grade component was evident in juxtacortical portion of the tumor [11]. Okada et al. reported that intramedullary involvement is a sign of higher-grade lesion and when present, usually does not involve more than one quarter of the intramedullary canal diameter [3]. The intramedullary involvement is reported to correlate with metastasis, local recurrence and worse prognosis by several authors, however this information was contradicted by some studies [2-4,7,12,14]. We recommend hemicortical resections in cases with a maximum circumferential extension of <50% and intramedullary involvement of <25%.

The neurovascular involvement was found more frequently in patients with higher maximum circumferential extension percentage ( $p=0.036$ ) and intramedullary involvement ( $p=0.041$ ). The assessment of soft tissue extension in primary parosteal osteosarcoma, which is reported as a significant determinant of the grade, should include meticulous evaluation of MRI [3,11,15]. Achieving wide margins in the popliteal region is reported to be difficult without sacrificing the neurovascular bundle [15]. Our study showed that the presence of neurovascular involvements was related with the incidence of metastatic disease, deep infections and complication related surgeries.

Complete excision is reported to be the mainstay of the treatment in parosteal osteosarcomas [2-4,6,7,10,12,15]. It is noted that tumor positive margins were associated with metastasis and local recurrences even after two decades [2,9]. Lewis et al. stated that

tumor free margins remains the critical factor determining overall prognosis [12]. Our study demonstrated that the maximum periosteal circumferential extension percentage of the parosteal osteosarcoma on preoperative MRI could be a good indicator for determining involvement and planning wide resections. Our study also suggested that these lesions have tendency to spread over the bone segment in all dimensions as they become larger thus we recommend meticulous evaluation of the horizontal sections of the MRI for planning resections. Our study suggested that the maximum periosteal circumferential extension percentage of the lesion that exceeds 50% of the bone at horizontal plane could be an indicator of intramedullary involvement. The literature suggests that the accurate definition of the margins on preoperative multiplanar MRI is important for successful wide resection in parosteal osteosarcoma [11,16]. Amputations are recommended in patients with large circumferential tumor with involvement of the neurovascular structures or contaminated surrounding soft tissue as a result of previous interventions [3].

Overall, our results were consistent with earlier studies by means of oncological outcomes. The 10-year overall survival was reported as 80-91% in various series, which, some authors included dedifferentiated cases [3,4,7]. Including dedifferentiated cases, our study suggested a 5-year overall survival as high as 92.3%. The local recurrence rate of parosteal osteosarcoma was reported within a range of 0-57% in published series [1,3,4,6,7,12,15]. Present study not only included primary cases but also improper interventions and misdiagnosed cases, have

demonstrated a 5-year local recurrence-free survival ratio of 86.2%. The metastasis rates were reported ranging 8-14.8% in previous series [3,4,7]. Okada et al. suggested 11% cumulative probability rate within 10-year [3]. The distant metastasis patients in our series was 2 with a 5-year metastasis-free survival of 86.2%. One patient who had lung metastasis at the time of diagnosis had history of previous biopsies in elsewhere center. The presence of delayed diagnosis and improper interventions have decreased metastasis free survival ratios in our series.

This study had several limitations. This study is primarily based on MRI findings and their prognostic importance. Some misdiagnosed patients have applied previous operations without the diagnosis of parosteal osteosarcoma. To overcome a potential bias, the evaluations were completed after the diagnosis of parosteal osteosarcoma in our clinic.

The reliability of needle biopsy sampling which, may cause misdiagnoses or improper interventions, is controversial in parosteal osteosarcomas. Previous interventions should be questioned in details especially in lesions, which are in close relation with neurovascular structures. When planning the surgery, the orthopaedic surgeon must consider the lesions extent of intramedullary involvement, neurovascular bundle proximity and maximum periosteal circumferential extension on MRI. Particularly the evaluation of maximum circumferential extension on preoperative MRI is crucial in determining the resection margins.

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