



Which one of the benign tumors and tumor-like lesions located in long bones needs prophylactic fixation during surgery?

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In the management of benign and tumor-like lesions, bony defects have been the subject of main dispute among orthopedic surgeons for many years. Benign bone tumors or tumor-like lesions often weaken bones and predispose to pathological fractures. The goal of the surgery is to prevent tumor recurrence and to allow the restoration of bone strength. Adjuvant measures such as phenol instillation or cryotherapy with liquid nitrogen may additionally be applied due to their chemical and physical effects improving the local effect of curettage.^[1-5]

Large bone cavities have been reinforced with autologous bone grafts, allografts, polymethylmethacrylate bone cement and bone substitutes.^[6] Factors affecting the biomechanics of

ABSTRACT

Objectives: This study aims to define the simultaneous prophylactic fixation indications of benign tumors and tumor-like lesions located in long bones that were treated by curettage and grafting/cementing.

Patients and methods: Fifty-six patients (33 males, 23 females; mean age 30.9±15.9; range, 15 to 65 years) who were treated by curettage and grafting or cementation for their benign tumors or tumor-like lesions in long bones between January 2013 and June 2016 were retrospectively analyzed. Age, sex, anamnesis and physical examination findings, histopathologic diagnosis, lesion localization, pre- and postoperative imaging results and follow-up data were all analyzed. The patients were divided into two groups as those with and without postoperative fracture.

Results: The most common localization was femur (38%). The mean tumor diameter was 6.8±2.2 (range, 2.6 to 12.6) cm and volume was 58.3±45.0 (range, 6 to 177) cm³. Postoperative fracture occurred in 14 patients. The lesion diameter and volume of the patients in postoperative fracture group were significantly higher compared to group without postoperative fracture (p=0.034 and p=0.004, respectively). A volume value greater than 67 cm³ and ages over 35 years were found to be associated with a higher rate of fracture for all lesions.

Conclusion: In the postoperative period, patients with benign tumors or tumor-like lesions of long bones had a higher fracture risk if the volume value was greater than 67 cm³ and the age was over 35 years. Prophylactic fixation may be suggested for these patients.

Keywords: Benign and tumor-like lesions, bone grafts, curettage, postoperative fracture.

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bone and leading to pathological fractures are bone defect size, biological behavior of bone lesion and the anatomic location of the lesion. Diagnosis and estimation of fracture at risk with its decision for prophylactic fixation are difficult. Many authors recommend prophylactic osteosynthesis for all impending fractures.^[7] But the fixation materials lead

to problems in assessment of tumor recurrence and follow-up. During the follow-up, if a fracture occurs in patients who did not undergo prophylactic fixation, these patients need reoperation and this imposes additional cost. In this study, we aimed to define the simultaneous prophylactic fixation indications of benign tumors and tumor-like lesions located in long bones that were treated by curettage and grafting/cementing.

PATIENTS AND METHODS

This retrospective study included 56 patients (33 males, 23 females; mean age 30.9 ± 15.9 ; range, 15 to 65 years) of benign and tumor-like lesions of the long bone who were treated in the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital with curettage, grafting or cementation between January 2013 and June 2016. The indications for surgical treatment of these lesions were impending pathological fracture due to significant endosteal erosion of the cortex with marked thinning of the wall and persistent pain. The data were supplied from medical records and all the patient radiograms were examined to determine whether there had been any healing of

the defect or any complications had developed. The mean follow-up duration was 19.5 ± 5.0 (range, 16 to 36) months. The most common histological diagnosis was enchondroma in 18 patients (Figure 1a), followed by simple bone cyst (SBC) in 17, aneurysmal bone cyst (ABC) in seven, giant cell tumor (GCT) in six, fibrous dysplasia (FD) in five and chondroblastoma in three patients (Table I). The study protocol was approved by the Dr. Abdurrahman Yurtaslan Ankara Oncology Health Practice and Research Center Ethics Committee (date: 04.09.2019, no: 2019-08/347). A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Lesions were located in the upper extremity (humerus, radius) in 23 patients and in the lower extremity (femur, tibia) in 33 patients. Preoperative biopsy was performed in all locally aggressive lesions except the SBCs and FD. Magnetic resonance imaging (MRI) and X-rays in all patients were retrieved from the treatment files to see the intraosseous extent and involvement of soft tissue. The preoperative MRIs of related lesions (coronal and sagittal views) were examined and measurements of size and volume of the lesions were recorded.

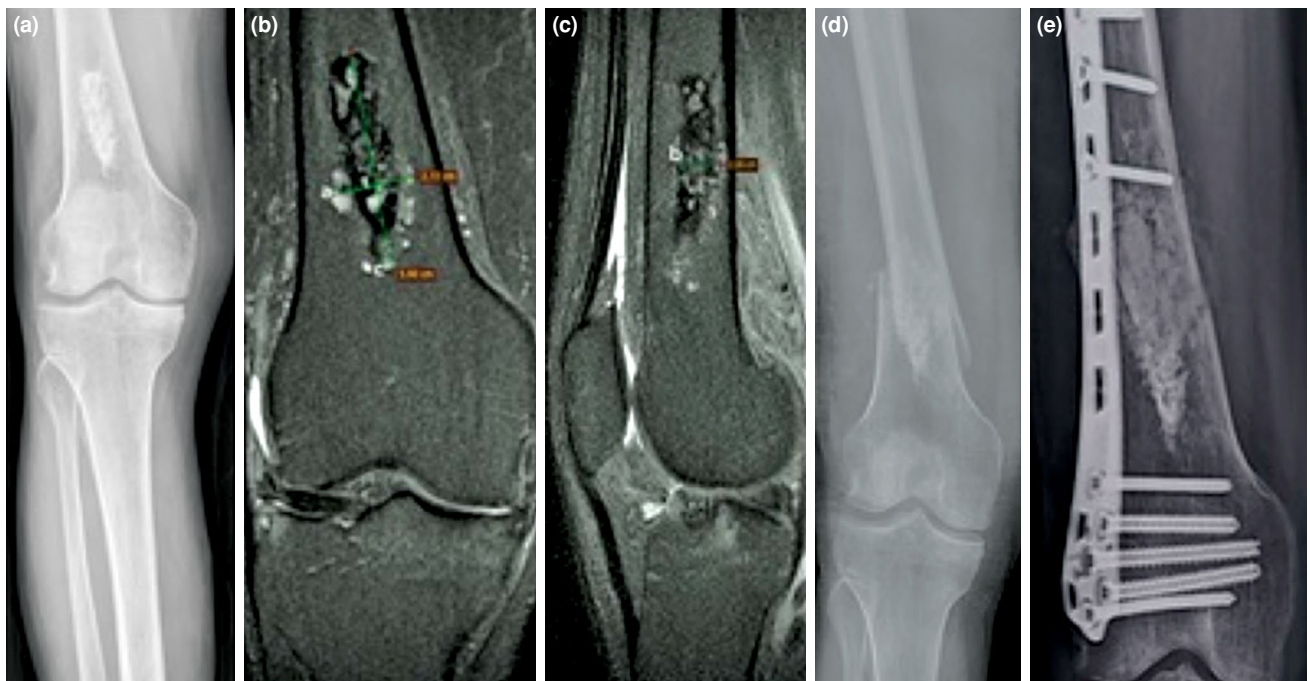


FIGURE 1. Case presentation representing a 65-year-old male with enchondroma of the right distal femur. (a) Anteroposterior radiographs showing enchondroma of right distal femur. (b, c) Same patient's coronal and sagittal MRI of distal femur showing the enchondroma lesion with prominent intramedullary involvement. View (a= width, b= depth, and c= height). (d) Fracture image after curettage and bone grafting. (e) Image showing open reduction and internal fixation with plates and screws.

MRI: Magnetic resonance imaging.

TABLE I
Baseline demographics of patients

Characteristic	Postoperative fracture														p			
	No (n=42)							Yes (n=14)								Total (n=56)		
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median		Min-Max		
Age (year)			27.9±14.5	20	15-63			40.1±16.7	43	15-65			30.9±15.9	23.5	15-65	0.020*		
Sex																0.433**		
Female	19	45.2				4	28.6				23	41.1						
Male	23	54.8				10	71.4				33	58.9						
Complaints																0.201**		
Pain	30	71.4				13	92.9				43	76.8						
Incidental	12	28.6				1	7.1				13	23.2						
Histological diagnosis																NA		
Simple bone cyst	13	31.0				4	28.6				17	30.4						
Enchondroma	10	23.8				8	57.1				18	32.1						
Aneurysmal bone cysts	7	16.7				0	0				7	12.5						
Fibrous dysplasia	5	11.9				0	0				5	8.9						
Giant cell tumors	4	9.5				2	14.3				6	10.7						
Chondroblastoma	3	7.1				0	0				3	5.4						
Place																0.047**		
Humerus	19	45.2				1	7.1				20	35.7						
Radius	2	4.8				1	7.1				3	5.4						
Femur	12	28.6				9	64.4				21	37.5						
Tibia	9	21.4				3	21.4				12	21.4						
Extremity																0.041**		
Upper extremity	21	50				2	14.3				23	41.1						
Lower extremity	21	50				12	85.7				33	58.9						
Diameter of the lesions (cm)			6.4±2.1	6.35	2.6-11.7			7.9±2.3	7.15	4.9-12.6			6.8±2.2	6.5	2.6-12.6	0.034*		
Volume of the lesions (cm ³)			47.4±37.4	38	6-167			91.0±51.2	80.5	16-177			58.3±45.0	45.5	6.0-177.0	0.004*		
Follow-up duration (month)			19.5±5.2	18	16-36			19.3±4.4	18	16-32			19.5±5.0	18.0	16.0-36.0	0.749*		

SD: Standard deviation; Min: Minimum; Max: Maximum; NA: Not available; * Mann-Whitney U test; ** Chi-square test.

The volume calculations were performed as follows, where A=width, B=depth, and C=height.

Cylindrical defect=ABC×0.785, i.e. $(\pi \times A/2 \times B/2 \times C)$.

Spherical defect=ABC×0.52, i.e. $(4/3 \times \pi \times A/2 \times B/2 \times C/2)$ (Figure 1b, c).^[8,9]

The most appropriate formula between these two was used depending on the perceived shape of the defect (i.e. The neck of the femur was considered as spherical, while metaphyseal and diaphyseal regions were considered as cylindrical).

All lesions were treated with intralesional curettage followed by bone grafting or cementation. Surgery involved intralesional curettage through a cortical window large enough over the lesion followed by high-speed power burring, brushing and pulse lavage of the lesion. The curettage was considered complete when normal smooth cortical bony surface with punctate bleeding and medullary cavity was visible. Every nook and corner was curetted repeatedly with burr and the electric cauterly to leave no macroscopic disease anywhere in the cavity. Fluoroscopy was taken to control in patients with large tumor volume after the curettage. The cavity was abundantly irrigated using jet lavage with normal saline and hydrogen peroxide. If extension into soft tissues was seen, the entire pseudocapsule was dissected circumferentially and excised completely. The curetted material was sent for routine histopathological examination.

Adjuvant treatment was given in 31 patients (GCT, ABC, enchondroma): an aqueous solution of phenol was applied on the curetted wall with a sponge, and then rinsed in pure alcohol; this procedure was continued for 20 min. 25 patients underwent only adjuvant treatment after curettage with electric cauterly. Adjuvant treatment before filling the intraosseous cavity included filling of the lesion with allograft (n=43) and bone cement (n=11), autograft and allograft (n=2). Passive range of motion exercises and partial weight bearing with a pair of axillary crutches were allowed as long as the pain was tolerated on the postoperative fourth or fifth day and continued for two weeks. This was followed by cane support for three to four weeks. After a total period of minimum six weeks, full weight bearing without support was allowed depending on the size of the lesions and the radiological features. All of our patients were on full weight bearing after eight (range, 6 to 12) weeks. Passive shoulder movements started on the postoperative second day if the case was related to upper extremity. Treatment and follow-up characteristics of patients are provided in Table II.

Patients treated for upper extremity were allowed to perform all routine daily activities starting from postoperative eighth week. Plain radiograms were taken at two-month intervals for at least 16 months. The outcomes were based on serial radiographic consolidation of the lesions along with subjective

TABLE II							
Treatment and follow-up characteristics							
	Postoperative fracture				Total (n=56)		p
	No (n=42)		Yes (n=14)				
	n	%	n	%	n	%	
Adjuvant treatments							0.227*
Curettage and cauterly	21	50	4	28.6	25	44.6	
Curettage, cauterly and phenol	21	50	10	71.4	31	55.4	
Filling of the lesion							NA
Allograft	34	81	9	64.3	43	76.8	
Autograft and allograft	2	4.7	0	0	2	3.6	
Bone cement	6	14.3	5	35.7	11	19.6	
On full weight bearing time							0.731*
6 th week	8	19	2	14.3	10	17.8	
8 th week	16	38.1	7	50	23	41.1	
>10 th week	18	42.9	5	35.7	23	41.1	
Local recurrences							NA
Yes	8	19	0	0	8	14.3	
No	34	81	14	100.09	48	85.7	

NA: Not available; * Chi-square test.

clinical assessment and function in the patient records.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as number and percentage, while continuous variables were expressed as mean±standard deviation and median (min-max) values. The relevance of continuous variables to normal distribution was evaluated using the visual (histogram and probability graphics) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). For categorical variables, whether there was a difference with respect to frequency between the groups was compared using the chi-square test. The Mann-Whitney U test was used for the comparison of abnormally distributed data between the groups. The Wilcoxon test was used to evaluate the change in pain score before and after treatment. Receiver operating characteristic (ROC) curve analysis was used to determine whether the diameter and volume of the lesions and age were optimum cut-off values in distinguishing patients with postoperative pathological fractures. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of significant limit values were estimated. Multivariate logistic regression analyses were used to assess the effect of independent predictors on postoperative pathological fractures. These data were presented as odds ratio (OR) with 95% confidence intervals (CIs). A *p* value of <0.05 was considered statistically significant.

RESULTS

Twenty-one (38%) lesions were located in the femur (femur neck [n=2], distal femur [n=14], proximal femur [n=5]), 20 (36%) were in the humerus (proximal [n=12], diaphysis [n=6], distal [n=2]), 12 (21%) were in tibia (proximal [n=6], distal [n=6]) and three (5%) were in the distal radius. The most common complaint was pain in 43 patients. The diagnosis was incidental in 13 patients. The mean diameter of the lesions in all patients was 6.8±2.2 (range, 2.6 to 12.6) cm. The mean volume of the lesions was 58.3±45.0 (range, 6 to 177) cm³. Fourteen patients had postoperative fractures, all within three months of their operation. Among these 14 patients, seven of the fractures were located in the distal femur, two in the proximal femur, one in the humerus diaphysis, one in the proximal radius, two in the distal tibia, and one in the proximal tibia. In cases of fracture (14 patients), mean diameter of the lesions was 7.9±2.3 (range, 4.9 to 12.6) cm while

mean volume of the lesions was 91.0±51.2 (range, 16 to 177) cm³. Ten patients with postoperative fractures required internal fixation (Figure 1d, e). The other fractures (n=4) were stable fractures and treated conservatively in plaster with restriction of weight bearing.

Particular demographic characteristics of 42 patients who did not develop postoperative fractures and 14 patients who developed postoperative fractures were compared in Table I. The median age of the patients who developed postoperative fracture was statistically significantly higher than those without postoperative fracture (*p*=0.020). Sex and complication states were found similar between groups (*p*=0.433 and *p*=0.201, respectively). Lesions in 85.7% of the group without postoperative fracture and 50.0% of the group with postoperative fracture were localized in lower extremity and found to be statistically significant (*p*=0.041). Treatment features and the time elapsed till full weight bearing were similar in both groups (*p*=0.227 and *p*=0.731, respectively) (Table II).

Local recurrences developed in the follow-up period with a mean 21.4 (range, 17 to 36) months in eight (14.3%) patients (n=3, SBC; n=2, GCT [one Grade 2 and one Grade 3]; n=2, enchondroma;

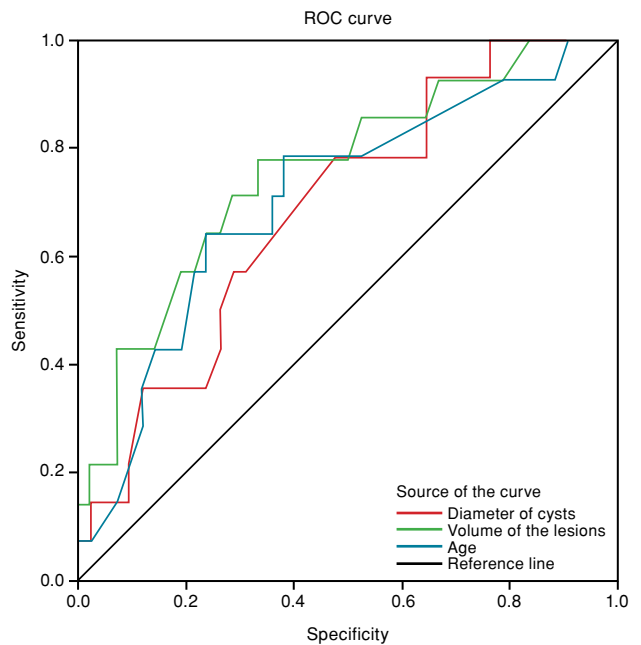


FIGURE 2. Receiver operating characteristic curve for lesion diameter, age and volume as predictor of postoperative pathological fractures. ROC: Receiver operating characteristic.

TABLE III

Statistical parameters of various diagnostic approaches for predicting postoperative pathological fractures with receiver operating characteristic curve analysis

Parameter	AUC (95% CI)	<i>p</i>	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Diameter of the lesions	0.690 (0.538-0.842)	0.035	≥7	57.1	71.4	40.0	83.3
Volume of the lesions	0.759 (0.611-0.906)	0.004	≥67	71.4	71.4	45.5	88.2
Age	0.707 (0.547-0.868)	0.021	≥35	64.3	73.8	45.0	86.1

AUC: Area under curve; CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value.

TABLE IV

Multivariate logistic regression analysis on risk factors for postoperative pathological fractures during follow-up period

	Multivariate logistic regression analysis model*		
	Adjusted OR	95% CI	<i>p</i>
Age (≥35 vs <35 years)	11.6	1.5-1.4	0.020
Extremity (lower vs upper)	2.1	0.3-15.4	0.467
Volume of the lesions, (≥67 vs <67 cm ³)	7.5	1.2-49.2	0.035
Complaints (pain vs. incidental)	5.8	0.5-65.9	0.154
Adjuvant treatments (curettage and cauterly vs. curettage, cauterly and phenol)	0.4	0.1-3.3	0.419

CI: Confidence interval; OR: Odds ratio; * Variables with *p*<0.2 as determined by univariate analysis were entered into multivariate logistic regression mode; Diameter of lesion was not included in regression analysis due to strong correlation (*r*=0.842) between volume and diameter of lesions.

and *n*=1, ABC. Seven patients had undergone repeated curettage and cauterizing; two of them required subsequent augmentation with autograft and one patient with a lesion localized in distal radius was reconstructed with allogeneous fibula and internal fixation. Endoprosthetic replacement was performed in a patient (distal femur) who was diagnosed with GCT and in whom we thought the curettage treatment would be insufficient.

None of the patients had deep infection at wound site while one patient had superficial infection which responded to prolonged antibiotic therapy.

The median lesion volumes were 38.0 (min 6.0-max 167) and 80.5 (min 16.0-max 177) cm³ in the groups without and with postoperative fracture, respectively. Lesion volume was significantly higher in the group with postoperative fracture (*p*=0.04). The median lesion diameters were 6.35 (min 2.6-max 11.7) and 7.15 (min 4.9-max 12.6) cm in the groups without and with postoperative fracture, respectively. This difference was statistically significant (*p*=0.034) (Table I). Postoperative fracture prediction power of characteristics such as age, lesion volume and lesion diameter was evaluated with ROC analysis (Figure 2). Area under the curve (AUC), cut-off,

sensitivity, specificity, PPV and NPV belonging to the ROC analysis were all presented in Table III. All three parameters were found to have significant power of prediction. The AUC=0.759 (*p*=0.004) belonging to lesion volume was found to be higher than the lesion diameter, indicating that the highest predictive power belonged to lesion volume. The most sensitive and specific cut-off values according to ROC analysis were 7 cm for lesion diameter, 67 cm³ specific for lesion volume and 35 for age. The effect of these parameters on patients for postoperative fracture was evaluated with multivariate logistic regression analysis (Table IV). Variables whose association with postoperative fracture at the univariate analysis showed *p*<0.200 were entered in the multivariate logistic regression model, which was used to identify factors independently associated with postoperative fracture. Patients aged over 35 years had fracture risk (OR): of 11.6 (95% CI: 1.5 to 51.4, *p*=0.020), and tumor volume equal to or higher than 67 cm³ had fracture risk of OR: 7.5 (95% CI: 1.2 to 49.2).

DISCUSSION

Treatment of patients with benign and tumor-like lesions has been a challenge for orthopedic surgeons. There are two main reasons for this: the first is

insufficient curettage, and curettage of benign and tumor-like lesions is performed through a bone window large enough for the tumor to be curated. With small bone windows, complete excision may not be easily achieved for large or deep-seated tumors, which may consequently result in a higher local recurrence rate. Second, increased tumor length also correlates with increased risk of pre- or postoperative pathological fracture and makes the surgery more difficult. Addition of internal fixation has disadvantages such as prolonged operative time, blood loss, more tissue injury, higher infection rates, and chronic pain due to tissue irritation. In addition, fixation materials lead to problems in the assessment of tumor recurrence and follow-up.^[8-10] In this study, we evaluated patients who needed prophylactic fixation during surgery, considering the factors affecting the risk of fractures. We concluded that prophylactic internal fixation should be performed particularly in lesions over 67 cm³ and if the patient age is over 35 years.^[11]

Another concern is that need for prophylactic fixation may result in changes risk of postoperative fracture; therefore, the addition of internal fixation should be carefully planned. It is difficult to detect the recurrence of benign and tumor-like lesions in patients undergoing fixation since the light reflection in imaging studies of patients with prophylactic fixation is another problem, while filling the defect (cement or graft) with or without fixation makes this problem even more challenging. This implies the need to be more selective when deciding on the necessity of fixation particularly in tumor-like lesions.^[7,8]

Hirn et al.^[8] showed a strong correlation between risk of postoperative fracture and both size and volume of the lesion. The average size of the lesions that fractured postoperatively was 108 cm³, while the average size was 58 cm³ for the lesions that did not fracture ($p=0.003$). Curettage alone without an allograft or bone substitute may be used, but a higher rate of complications was found for tumors with a volume greater than 60 cm³. Kundu et al.^[12] also showed that the risk of fracture was lower in long bones and pelvic bones with lesions with volume of less than 70 cm³, compared to those with lesions with volume of larger than 70 cm³. They found that the average size of the lesions that fractured in long bones was 126.52 cm³ while the average size was 49.352 cm³ for the lesions that did not fracture. Review of serial radiograms revealed that while the smaller lesions filled up completely, the larger ones (70 cm³) tended to heal initially by

thickening of the cortex and then by development of septae running across the defect. However, this has raised concerns about the healing quality and time. Zekry et al.^[13] reported that internal fixation was indicated only in three cases with large lesions that presented with preoperative impending pathological fracture due to significant endosteal erosion of the cortex and marked thinning of the cortical wall in 27 cases located in proximal femur.

In our experience, lesions larger than 67 cm³ have greater risk of complications while smaller lesions have lower risk. Also, there is an increase in fracture rates in lesions with diameters of more than 7 cm. The median age of the patients who developed postoperative fracture was higher than those without postoperative fracture. Bone strength, bone architecture, slow bone turnover, possible bone mineral density problems, or osteoporosis history also increase fracture risk.^[14] Considering that bone lesions are spherical or cylindrical, we assume that area measurement as volume is more significant in detecting the fracture risk.

The development of postoperative fractures may be multifactorial. For this reason, multivariate logistic regression analysis was performed in univariate analyses to differentiate confounding situations that might be effective on fracture development. Thus, we wanted to show how effective the risky conditions are for fracture development by presenting adjusted OR by univariate analysis. Although univariate analysis indicated that lesion location might be effective on fracture development, multivariate logistic regression analysis showed that age and tumor volume were the most effective risk factors on the condition. Although it was concluded in the univariate analysis that postoperative fractures were more common in lesions localized in the lower extremities ($p=0.041$), it was understood that localization in extremity could be a confounding factor in multivariate logistic regression analysis ($p=0.467$). Multivariate logistic regression analysis has shown us that in fracture occurrence, tumor size and patient age are more contributing than extremity localization.

This study has some limitations. First is the evaluation of benign aggressive and benign tumors together to reach a statistically significant number. Assessment of tumors of different localizations of bone together such as femoral neck and diaphysis of femur is also a limitation. Moreover, during surgery, curettage is applied to the cortical walls adjacent to the lesion. This causes cortical thinning in most patients. When evaluating patients, cortical

involvement was not ignored, while the amount of erosion was not measured. This is another limitation of the study. Thus, further multicentric studies are needed to reach more patients.

In conclusion, prophylactic internal fixation should be performed in lesions with volumes of more than 67 cm³ and if the patient is aged over 35 years. To predict fracture risk in patients; the age of the patient, tumor localization, tumor volume, the area of tumor involvement of the cortex, patient compliance, and similar factors should be interpreted and evaluated together.

Declaration of conflicting interests

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