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Title: Post-metastasis survival in high-grade extremity osteosarcoma: A retrospective analysis of prognostic factors of 126 patients.

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Abstract

Background: Survival rate of patients with metastatic osteosarcoma remains poor although the prognosis of localized osteosarcoma has significantly improved with the introduction of combination chemotherapy. However, prognostic factors predictive of post-metastasis survival in high-grade osteosarcoma have not yet been fully established.

Questions/purposes: In this study, we analyzed (1) post-metastasis survival in high-grade extremity osteosarcoma patients and (2) its prognostic factors.

Materials and Methods: A retrospective review was conducted on 126 patients with metastatic osteosarcoma. The study population consisted of 70 men and 56 women, with a mean age of 21 years (range: 4–75 years). The median overall and post-metastasis follow-up period was 36 months (range: 6–293 months) and 20 months (range: 6–245 months), respectively. Thirty-three patients (26%) had metastasis at diagnosis. Lung was the most common metastasis site, accounting 113 of 126 metastases (91%). Complete surgical removal of the first metastatic lesion was performed in 78 patients (62%).

Results: Five-year overall post-metastasis survival rate was 31% and median post-metastasis survival time was 22 months. Favorable prognostic factors in post-metastasis survival based on univariate analysis were complete metastasectomy ($P<0.001$), no local recurrence prior to metastasis ($P<0.001$), unilateral lung metastasis ($P=0.002$), pulmonary metastasis only ($P=0.018$), good histologic response to primary chemotherapy ($P=0.038$), primaries not in the proximal humerus or proximal femur ($P=0.002$), age under 30 years ($P=0.015$), and alkaline phosphatase level under 400 IU/L ($P=0.034$) (Table 1). After multivariate analyses, complete metastasectomy ($P<0.001$), no local recurrence prior to metastasis ($P=0.016$), pulmonary metastasis only ($P=0.006$), unilateral lung metastasis ($P=0.034$), and good histologic response to primary chemotherapy ($P=0.047$) retained prognostic significance (Table 2).

Conclusions: We identified several prognostic factors predictive of post-metastasis survival at the time of metastasis detection. Our results suggest that primary tumor related factor such as histologic response to chemotherapy as well as metastasis related factors such as complete metastasectomy, metastasis site, and metastasis burden are important prognostic factors in patients with metastatic osteosarcoma.

Key word: osteosarcoma, metastasis, survival, prognostic factors

Table 1. Univariate analysis of prognostic factors for post-metastasis survival.

	Number (%)	Median overall survival (months)	P - value
Surgical remission for metastasis			<0.001*
Yes	78 (61.9%)	46.2±16.1	
No	48 (38.1%)	11.4±1.6	
Local recurrence prior to metastasis			<0.001*
Present	5 (3.9%)	5.0±0.8	
Absent	121 (96.1%)	23.9±3.4	
Laterality of lung metastasis			0.002*
Unilateral	57 (50.4%)	41.6±15.4	
Bilateral	56 (49.6%)	17.1±2.6	
Metastasis site			0.018*
Lung only	102 (80.9%)	26.0±5.1	
Others	24 (19.1%)	12.7±2.8	
Post-chemotherapy necrosis			0.038*
<90% or pasteurization	97 (76.9%)	20.8±3.1	
≥90%	29 (23.1%)	63.5±22.5	
Primary tumor site			0.002*
Proximal femur or proximal humerus	24 (19.0%)	12.7±3.6	
Others	102 (81.0%)	26.0±5.6	
Age			0.015*
< 30 years	102 (80.9%)	24.1±6.7	
≥30 years	24 (19.1%)	14.8±5.0	
Alkaline phosphatase			0.034*
< 400 IU/L	99 (89.1%)	23.9±2.9	
≥ 400 IU/L	12 (10.8%)	10.1±2.4	

*: statistically significant value

Table 2. Multivariate analysis of prognostic factors for post-metastasis survival.

	HR (95% CI)	P - value
Local recurrence prior metastasis		0.016*
Present	8.4 (1.5 – 47.0)	
Absent	1 (Ref.)	
Surgical remission for metastasis		<0.001*
No	3.5 (1.9 – 6.2)	
Yes	1 (Ref.)	
Metastasis site		0.006*
Others	3.3 (1.4 – 7.7)	
Lung only	1 (Ref.)	
Post-chemotherapy necrosis		0.047*
<90% or pasteurization	1.9 (1.0 – 3.8)	
≥90%	1 (Ref.)	
Laterality of lung metastasis		0.034*
Bilateral	1.8 (1.0 – 3.1)	
Unilateral	1 (Ref.)	

*: statistically significant value

HR: hazard ratio

CI: confidence interval

Ref.: reference