

Patterns of Local Recurrence and Metastatic Progression Following Treatment of Bone Sarcomas

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Background

The potential for local recurrence and pulmonary metastasis following treatment of primary bone sarcomas necessitates careful patient follow-up; however, minimal data exists regarding the incidence and timing of these events, and the frequency of optimal surveillance remains uncertain.

Methods

The study population consisted of 665 patients who underwent resection of a primary, non-metastatic bone sarcoma at a single tertiary referral oncology center between 1989 and 2010. Prospective records were reviewed for sarcoma type and histologic grade, as well as time and site of any disease recurrence. With patients stratified by sarcoma grade, Kaplan-Meier survival curves were constructed for the endpoints of local recurrence and metastasis, and log rank tests were used to compare the rates of these events in each group. Cox regression analysis was also performed to evaluate and control for patient age, tumor size, tumor location, and surgical margins as potential risk factors for disease progression. Finally, osteosarcoma and chondrosarcoma were analyzed separately because these were the two most common diagnoses and were hypothesized to behave distinctly.

Results

With a mean follow-up of 89.8 (range 12-298) months, we observed a total of 66 (10%) cases of local recurrence and 179 (27.0%) cases of metastasis, most of which were pulmonary (n= 138, 77.1%).

Sarcoma grade significantly influenced the timing of local recurrence but not the overall incidence; 78.6% of grade 1, 83.3% of grade 2, and 92.9% of grade 3 local recurrences occurred within the first 2 years, but 5-year local recurrence-free survival was not statistically different between these 3 groups (p=0.864) (Figure 1).

By contrast, both the incidence and timing of metastases were directly related to sarcoma grade ($p < 0.0001$) (Figure 2). Patient age, tumor location, and tumor location were not significant risk factors for disease progression; tumor size was statistically significant, but adjusting for this variable did not alter the crude differences in disease-free survival observed between sarcoma grades.

There were no metastatic events for grade 1 sarcomas after 3.25 years of follow-up, whereas metastasis of grade 2 and 3 sarcomas continued to develop until 10 years, with two cases of delayed events thereafter. The rate of pulmonary progression of intermediate grade tumors was significantly greater in osteosarcoma compared to chondrosarcoma ($p = 0.006$), particularly in the first 2 years.

Conclusions

Our findings suggest that the frequency and duration of surveillance following sarcoma treatment should be stratified according to histologic grade. We observed that local recurrence is not more common but is more likely to develop earlier with higher grade tumors. By contrast, increasing grade negatively impacted both the timing and incidence of lung metastasis. Patients with intermediate/high grade tumors should undergo pulmonary imaging until at least 10 years following treatment, while screening beyond 5 years may not be necessary for low grade tumors. Finally, the metastatic behavior of grade 2 osteosarcoma is more consistent with a high grade rather than an intermediate grade sarcoma, and more frequent screening may be indicated.

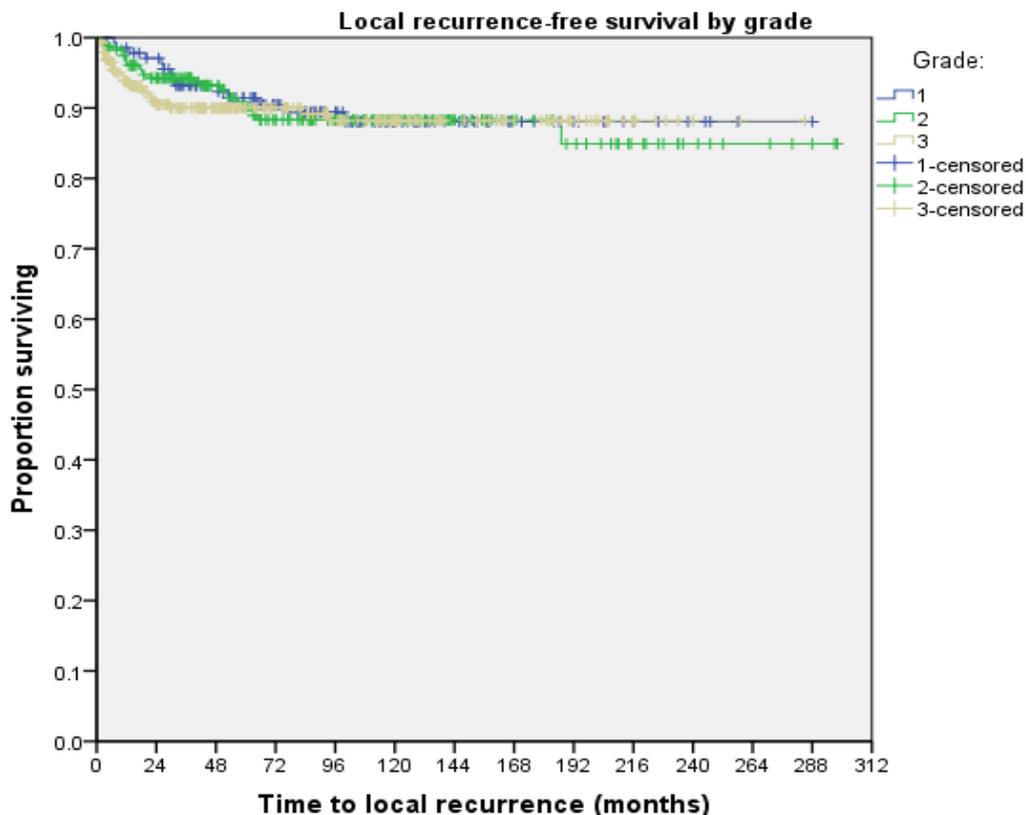


Figure 1. Rates of local recurrence for grade 1, 2, and 3 bone sarcomas.

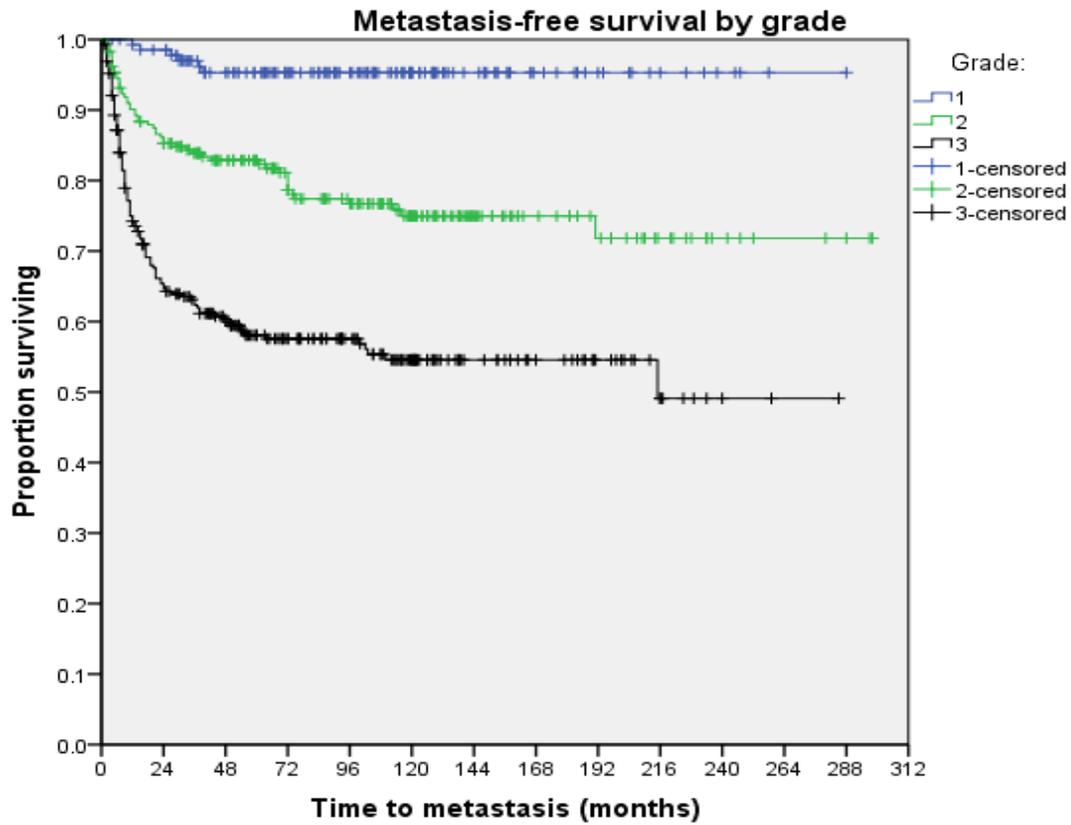


Figure 2. Rates of pulmonary metastasis for grade 1, 2, and 3 bone sarcomas.

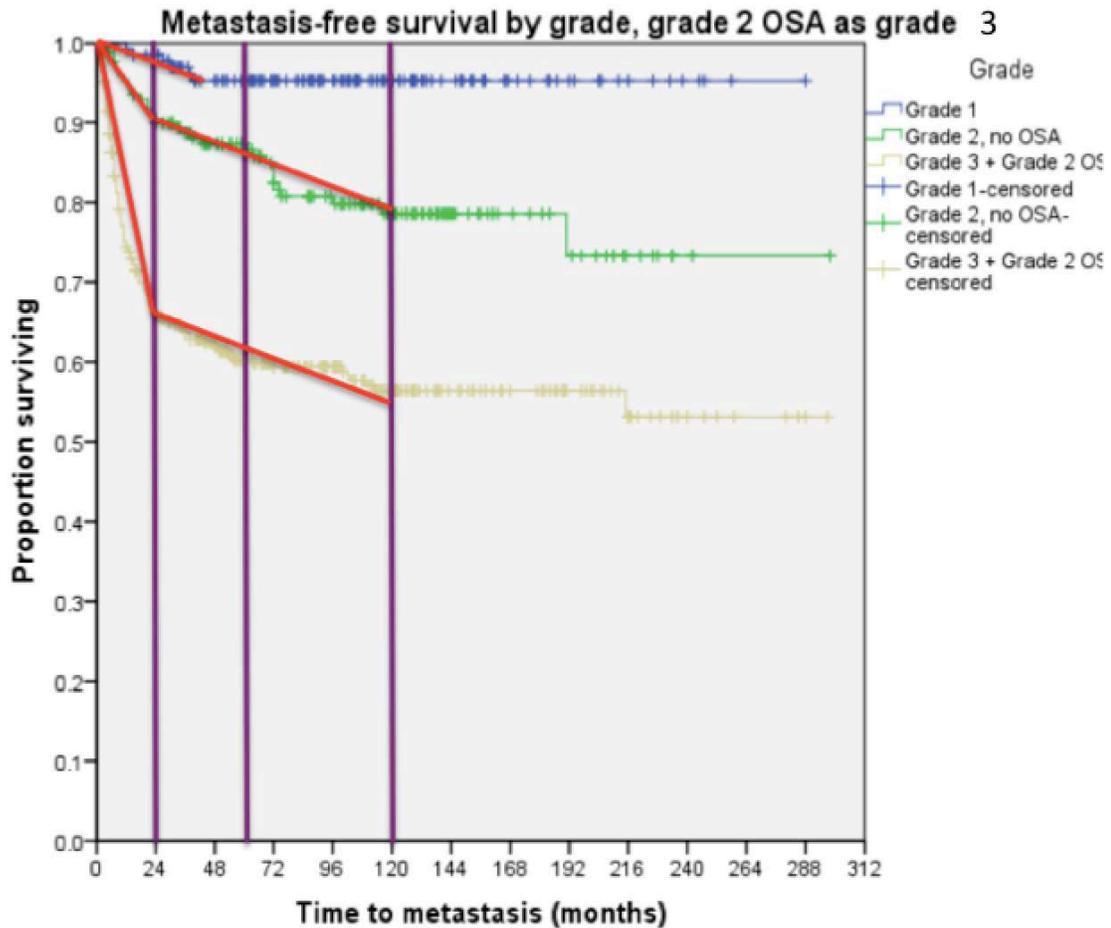


Figure 3. Metastasis-free survival by sarcoma grade with linear estimates (red lines) of event rates to guide surveillance frequency. The rates of early pulmonary metastasis differ significantly between groups, but the metastatic rate for grades 2 and 3 are similar after both 2 and 5 years. Of note, due to the accelerated rate of pulmonary metastasis in grade 2 osteosarcoma, these cases were included in the grade 3 rather than grade 2 category.