Poor Survival in Bone Sarcoma Patients with Metastasis to Bone at Diagnosis Highlights the Importance of Skeletal Staging

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**Background**

Staging of bone sarcomas classically includes a CT scan of the lungs and bone scintigraphy to evaluate their second most common sites of metastasis, respectively. Recent interest in modifying staging protocols, including PET/CT and whole-body MRI, has challenged convention and invites examination of the value of skeletal staging in modern practice.

**Questions and purposes**

This study therefore asked:

- What is the incidence of bone metastasis at diagnosis for bone sarcoma with and without lung metastasis?
- What factors are associated with bone metastasis at diagnosis?
- What is the overall survival for patients with metastasis to bone at diagnosis?

**Methods**

The National Cancer Database, a nationwide registry that includes 70% of all new cancers in the United States with 90% follow-up, was reviewed to identify 10220 patients diagnosed with primary chondrosarcoma, osteosarcoma, or Ewing sarcoma of bone from 2010-2015. Patients were excluded who did not have documented status of metastatic disease at diagnosis for bone (3%; n = 357) and lung (<1%, n = 8). A total of 9855 patients were included (chondrosarcoma, n = 4013; osteosarcoma, n = 4105; Ewing sarcoma, n = 1737), with median follow-up of 29 months. Multiple logistic regression analysis was performed after backwards selection for associations with bone metastasis at diagnosis. Unadjusted Kaplan-Meier survival analysis was conducted stratified by lung and bone metastases at diagnosis before comparison using the log-rank test and pairwise log-rank test for multiple comparisons.

**Results**

**Figure 1.** Location of distant metastatic disease at diagnosis by histology. A total of 9855 patients were included (chondrosarcoma, n = 4013; osteosarcoma, n = 4105; Ewing sarcoma, n = 1737). Patient demographic, clinicopathologic, and treatment characteristics are represented of a national sample.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.00</td>
<td>0.00</td>
<td>0.15</td>
</tr>
<tr>
<td>SES composite</td>
<td>1.22</td>
<td>0.92</td>
<td>0.38</td>
</tr>
<tr>
<td>Insurance</td>
<td>1.10</td>
<td>0.86</td>
<td>0.56</td>
</tr>
<tr>
<td>Tumor location</td>
<td>1.60</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>Histology</td>
<td>2.01</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>Other</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>&lt;=</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
<tr>
<td>High risk</td>
<td>4.38</td>
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<td>0.01</td>
</tr>
<tr>
<td>Low risk</td>
<td>1.12</td>
<td>0.99</td>
<td>0.46</td>
</tr>
<tr>
<td>&gt;</td>
<td>0.99</td>
<td>0.36</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Figure 2.** Multiple logistic regression analysis of factors associated with metastasis to bone at diagnosis for bone sarcomas. Unstandardized odds ratios are displayed on a logarithmic scale with 95\% confidence intervals. CI indicates confidence interval; SES, socioeconomic status, which was stratified into quartiles 1-4, with higher number indicating greater education and income at the zip-code level.

**Figure 3.** Unadjusted overall survival analysis stratified by presence or absence of lung and bone metastases at diagnosis. Kaplan-Meier survival curves are shown, with the number at risk for each group, for all cases (A), chondrosarcoma (B), osteosarcoma (C), and Ewing sarcoma (D). For all histologies, patients with lung and bone metastasis had worse survival than those with lung metastasis and no bone metastasis (for all histologies, \(p < 0.01\)).

**Conclusions**

This study highlights the importance of skeletal staging in bone sarcoma using a large cohort of patients from a recent, nationwide sample. Staging of the lungs alone in this population would have failed to recognize 25% of patients with metastatic disease at diagnosis for chondrosarcoma, 16% for osteosarcoma, and 35% for Ewing sarcoma. The addition of skeletal staging would leave 12% of metastatic disease at diagnosis unrecognized for chondrosarcoma, 8% for osteosarcoma, and 10% for Ewing sarcoma. Poor survival outcomes in patients with extrapulmonary metastatic disease necessitate early diagnosis to inform prognosis and guide treatment of the primary tumor. Based on these findings, skeletal staging at diagnosis should continue for bone sarcomas and imaging of other sites should be considered.