Decreased Tumor Percent Necrosis is Associated with Positive Final Margin Status in Osteosarcoma

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INTRODUCTION: Decreased tumor percent necrosis in osteosarcoma is indicative of a poor response to chemotherapy and has been associated with worse patient outcomes. Positive surgical margins following osteosarcoma resection are associated with an increased likelihood of local recurrence. To date, no study has primarily evaluated the relationship between tumor percent necrosis and surgical margin status in osteosarcoma. The purpose of this study was to evaluate the relationship between tumor percent necrosis and surgical margin status in osteosarcoma.

METHODS:

After receiving institutional review board approval, we queried our institution's orthopaedic oncology registry, which includes all patients treated for a musculoskeletal bone or soft tissue tumor at our single tertiary academic hospital since 1987. We identified all patients who received neoadjuvant chemotherapy, underwent primary surgical resection at our institution, had a confirmed final pathologic diagnosis of osteosarcoma, and had a histologically analyzed tumor percent necrosis documented. For the 255 patients included in this study, we retrospectively collected patient, tumor, treatment, and oncologic outcome data (Table 1). We analyzed the associations between tumor percent necrosis, surgical margin status, and event-free survival (EFS). We defined EFS as the time from definitive surgical resection to local recurrence, metastatic spread, death, or last date of oncologic follow up.

RESULTS: The median and mean tumor percent necrosis for all patients was 80% (IQR 40-95%) and 67% (SD 31%, range 0-100%), respectively. 89% of patients (228/255) had negative surgical margins, while 11% (27/255) of patients had positive surgical margins. The median tumor percent necrosis for patients with negative margins was 80% (IQR 45%-95%) while the median tumor percent necrosis for patients with positive margins was 60% (IQR 35%-85%). The mean tumor percent necrosis for patients with negative margins was 68% (SD 31%, range 0%-100%), while the mean tumor percent necrosis for patients with positive margins was 58% (SD 29%, range 5%-99%) (P = 0.024) (Figure 1). Decreased tumor percent necrosis was associated with decreased EFS (r = 0.125, P = 0.047) and positive final margin status was associated with decreased EFS (P = 0.018). Among patients with positive surgical margins, 33% (9/27) had lymphovascular invasion of tumor on final pathology, 70% (19/27) of patients had tumors with neurovascular bundle involvement, and 19% (5/27) patients had both lymphovascular invasion of tumor and tumors with neurovascular bundle involvement. Of note, 15% (4/27) of patients with positive surgical margins presented with a pathologic fracture.

DISCUSSION AND CONCLUSION: Margin status is often used as one measure of surgical performance in the resection of sarcoma. Though surgical execution is important, it is widely believed that factors inherent to tumor biology and behavior also contribute to margin status. These data show a decrease in tumor percent necrosis is associated with positive final margin status, and both decreased tumor percent necrosis and positive margin status are associated with decreased EFS. Though these findings are simply correlative and not causal, we hypothesize decreased tumor necrosis may lead to more viable cancer cells at the resection margin, representing another factor inherent to tumor biology, behavior, and treatment effect that may contribute to positive margin status, independent of surgeon performance.

Tumor Percent Necrosis and Final Margin Status

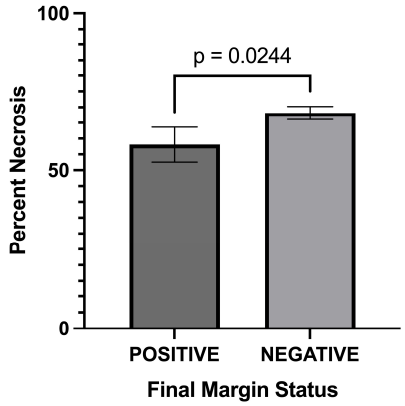

Table 1. Patient, tumor and treatment data

	n	%
Total	255	100%
Age (mean, SD)	23.4	16.2
Sex		
Female	104	40.8%
Male	151	60.2%
Race		
White	202	79.2%
Black	27	10.6%
Hispanic	15	5.9%
Asian	2	0.8%
Other/Multiple/Unknown	9	3.5%
Neoadjuvant Chemotherapy Regimen		
Methotrexate, adriamycin, cisplatin	157	61.6%
Adriamycin, cisplatin	57	22.4%
Other	23	9.0%
Unknown	18	7.1%
Tumor Location		
Femur	123	48.2%
Tibia	51	20.0%
Fibula	7	2.7%
Humerus	29	11.4%
Radius	1	0.4%
Ulna	1	0.4%
Pelvis	23	9.0%
Spine/Vertebrae	3	1.2%
Sacrum	2	0.8%
Rib Cage	3	1.2%
Other	12	4.7%
Tumor Subtype		
Chondroblastic	35	13.7%
Fibroblastic	18	7.1%
Giant Cell	2	0.8%
Osteoblastic	145	56.9%
Periosteal	5	2.0%
Small Cell	4	1.6%
Telangiectatic	8	3.1%
Other	20	7.8%
Unknown	18	7.1%