One Hundred Percent Tumor Necrosis is Associated with Survival in Ewing Sarcoma

Matthew Marley[1], Christopher Collier[2]

[1]Indiana University School of Medicine; [2]Indiana University School of Medicine, Department of Orthopaedic Surgery

Background and Objectives:
Ewing sarcoma is a primary malignancy affecting both bone and soft tissue. Following preoperative chemotherapy and surgical resection, histologic response (tumor necrosis) is correlated with patient survival. The most prognostic cutoff for tumor necrosis continues to be debated. The objective of this study was to explore several cutoffs and determine their prognostic value in a contemporary cohort of Ewing sarcoma patients.

Methods:
The National Cancer Database was used to identify 564 patients with osseous and soft tissue tumors in the Ewing sarcoma family from 2010 to 2015. All patients had documented preoperative chemotherapy, surgical resection, and vital status. Survival was stratified by tumor necrosis using Kaplan Meier analysis. 356 patients with osseous tumors were included in multivariate logistic and cox regression analyses to identify predictors of histologic response and survival, respectively.

Results:
In a combined soft tissue and osseous tumor cohort, there was a significant difference ($p = 0.01$, log-rank test) in overall survival between patients with 100% necrosis and patients with less than 100% necrosis. This was observed over the 5-year study period. Other cutoffs were not statistically different. In patients with osseous tumors, less than 100% necrosis was negatively associated with survival (HR 3.48 [95% CI 1.19-10.13]; $p< 0.05$), with only skip metastasis having a stronger negative association (HR 4.31 [95% CI 1.22-15.29]; $p< 0.05$). Male sex (OR 0.50 [95% CI 0.28-0.90]; $p<0.05$), tumors located in the axial skeleton (OR 0.30 [95% CI 0.12-0.77]; $p<0.05$), and positive surgical margins (OR 0.28 [95% CI 0.08-0.95]; $p<0.05$) were negatively associated with 100% necrosis.

Conclusion and Implications:
A cutoff of 100% tumor necrosis was associated with improved survival in Ewing sarcoma. This association was strong relative to other commonly used prognostic factors in osseous cases and is a valuable tool to counsel patients and guide future clinical trials.