

PAPER 2

Surgical staging of osteosarcoma: does incorporation of chemotherapy response improve prediction of local recurrence?

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BACKGROUND

Traditional staging systems for high grade osteosarcoma (Enneking, MSTS) are based largely on gross surgical margins and were developed before the widespread use of neoadjuvant chemotherapy. It is now widely accepted that microscopic margins and chemotherapy are predictors of local recurrence. However, neither of these variables are used in the traditional surgical staging and the precise safe margin distance is debated. Recently, a novel staging system utilizing a 2mm margin cutoff and incorporating percent necrosis was proposed and demonstrated improved prognostic value for local recurrence free survival (LRFS) when compared to the MSTS staging system. This staging system has not been validated beyond the original patient cohort.

QUESTION/PURPOSE

We propose to assess a surgical staging system utilizing percent necrosis and a 2mm margin cutoff in a cohort of patients with high-grade osteosarcoma, as well as evaluate the ability of additional variables to predict the risk of local recurrence and overall survival.

METHODS

A retrospective review of a prospectively collected database of all sarcoma patients between 1985 and 2021 at a tertiary sarcoma referral center was performed. All patients with high-grade osteosarcoma receiving neo-adjuvant chemotherapy and with no evidence of metastatic disease on presentation were isolated and analyzed. A minimum of two year follow up was used for surviving patients. A total of 225 patients were identified meeting these criteria. Univariate analysis was performed to evaluate variables that were associated with LRFS. Multivariate analysis is used to further analyze factors associated with LRFS on univariate analysis. A stepwise cox regression model was used to compare the MSTS and Birmingham staging systems.

RESULTS

The mean age at surgery was 31.78 (SD 15.7; range 13-77). There were 22 patients (11%) who had locally recurrent disease. Five-year DSS was 60.3%, and 5-year LRFS was 87.1%. Central tumor location ($p<0.001$), MSTS classification ($p<0.001$), Birmingham classification ($p=0.005$), and binary involved/uninvolved margin status ($p<0.001$) were significant predictors of 5-year LRFS in univariate analysis. Notably, percent necrosis was not a predictor of LRFS in this cohort ($p=0.85$). Only central tumor location (HR 3.26; CI 1.3-8.5, $p=0.002$) and binary involved/uninvolved margin status (HR 19.5; 3.1-123.7, $p=0.002$) remained significant predictors of 5-year LRFS on multivariate cox regression analysis. The Birmingham classification did not improve the predictive value of the MSTS classification in stepwise cox regression analysis.

CONCLUSION

In this cohort of patients with high-grade localized osteosarcoma, a surgical staging system based on percent necrosis and a 2mm margin cutoff did not improve upon the traditional MSTS system for predicting local recurrence. Central tumor location and involved surgical margins were the strongest predictors of 5-year LRFS. Chemotherapy response was not significantly associated with local recurrence.