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Evaluating Risk Factors for Skeletal-Related Events Among Patients with Bone Metastases: A Retrospective Analysis

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Published 03/19/2025

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Categories: Radiation Oncology, Palliative Care, Oncology
Keywords: asymptomatic bone metastases, bone metastases, prophylactic radiation, radiation, skeletal related event

How to cite this abstract
Leu J, Narra L, Gooley T, et al. (March 19, 2025) Evaluating Risk Factors for Skeletal-Related Events Among Patients with Bone Metastases: A Retrospective Analysis . Cureus 17(3): a1541

Abstract

Purpose

Skeletal-related events are a major source of morbidity and mortality across cancer types. Identification of patient-level and lesion-level variables, including cancer histology and lesion location, that are associated with the development of skeletal-related events and their association with overall survival would allow for more efficient and targeted preventive treatment.

Methodology

This retrospective cohort study with median of follow-up of 26.8 months among alive patients occurred at a single multi-site academic cancer center and included patients with solid tumors receiving systemic imaging for a diagnosis of bone metastases in February-March 2022 that had not received radiation within the past one year. Main outcomes included development of any skeletal-related events (and subset radiation for pain alone) and death from any cause. Patient-level factors included eligibility for a published phase 2 clinical trial of radiation to prevent skeletal-related events. A Cox proportional hazards model was utilized for survival analysis, and multi-state models were utilized to identify patient and lesion-level variables associated with skeletal-related events with death as competing risk.

Results

410 individuals were identified with an average age of 64 (55 – 74) years and 197 (48%) were male. Within this cohort 162 (40%) individuals developed skeletal-related events, including 75 (18.3%) with radiation for pain. All skeletal-related events (HR 1.98, 95% CI 1.47 – 2.67, p <0.001) and radiation for pain alone (HR 2.14, 95% CI 1.57 – 2.91, p <0.001) were both associated with decreased survival. On patient-level multivariable analysis, prostate histology (HR 1.74, 95% CI 1.12 – 2.70, p = 0.01) and radiation trial eligibility (HR 1.65, 95% CI 1.17 – 2.32, p = 0.004) were significantly associated with the development of skeletal-related events. On lesion-level univariable analysis, hip/acetabulum location (HR 2.55, 95% CI 1.16 – 5.60, p = 0.02) was significantly associated with any skeletal-related events relative to long bone.

Conclusions

Patients with prostate cancer and bone metastases in the hip/acetabulum location were most likely to develop SRE, which may inform further research into preventive strategies. The risk for death associated with radiation for pain alone was similar to any SRE, reinforcing the clinical relevance of radiation for pain in the SRE endpoint definition. This analysis also supports the validity of the trial's eligibility criteria in enriching for develop of SRE. Further prospective evaluation is warranted.