Antiresorptive Medications Prior to Stereotactic Body Radiotherapy for Spinal Metastasis are Associated with Reduced Incidence of Vertebral Body Compression Fracture

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Objectives: Antiresorptive drugs are often given to minimize fracture risk for patients with bone metastases, but data regarding optimal time or ability to reduce stereotactic body radiotherapy (SBRT)-induced fracture risk is limited. This study examines the association between antiresorptive drug use surrounding spinal SBRT and the incidence of vertebral compressive fracture (VCF) to provide information regarding the effectiveness of these agents and optimal timing of delivery.

Methods: Patients treated with SBRT for spinal metastases at a single institution between 2009-2020 were included. Kaplan-Meier analysis was used to compare cumulative incidence of VCF for those taking antiresorptive drugs pre-SBRT, post-SBRT only, and none at all. Cox proportional hazards and Fine-Gray competing risk models were used to compare those taking antiresorptive drugs with covariates of drug duration, cumulative dose, radiation dose per fraction, BMI, and total SINS.

Results: Of the 234 patients (410 vertebrae) analyzed, 49 (20.9%) were taking bisphosphonates alone, 42 (17.9%) were taking denosumab alone, and 25 (10.7%) were taking both. Kaplan-Meier analysis revealed a statistically significant lower VCF incidence for patients initiating antiresorptive drugs before SBRT compared to those taking none at all (4% vs. 12% at 1 year post-SBRT, p=0.045; and 4% vs. 23% at 2 years, p=0.008). On multi-variate analysis there was a clinically meaningful reduced risk of VCF in those initiating bisphosphonates prior to SBRT (74% reduction, p=0.208) and for those initiating denosumab prior to SBRT (61% reduction, p=0.301) compared to those initiating them after SBRT. Denosumab duration (HR: 0.87, 95%CI: 0.63-1.19, p=0.378) or dose (HR: 1.00, 95%CI: 0.99-1.00, p=0.644) as well as bisphosphonate duration (HR: 0.98, 95% CI: 0.91-1.15, p=0.739) or dose (HR: 0.99, 95% CI: 0.95-1.04, p=0.741) were not shown to have statistical or clinical significance on VCF incidence. However, a higher dose per fraction in those taking bisphosphonates was shown to have a 30% higher risk of VCF incidence (p< 0.001).

Conclusion(s): Initiating antiresorptive agents prior to SBRT may reduce the risk of treatment-induced VCF. Antiresorptive drugs are underutilized in patients with spine metastases and may represent a useful intervention to minimize toxicity and improve long-term outcomes in this patient population.