

Sarcopenia is a Predictor of Post-Radiation Pathologic Vertebral Compression Fracture and Overall Survival

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INTRODUCTION: Symptomatic spine metastases without recognized structural instability are commonly treated with radiotherapy. Pathologic vertebral compression fractures (VCFs) occur 11-41% of the time following stereotactic body radiotherapy (SBRT) and are a significant source of morbidity, often necessitating invasive interventions such as kyphoplasty or stabilization surgery. Current spine pathologic fracture prediction models rely on anatomic and clinical information but do not factor in patient metabolic status. Sarcopenia, a frequent consequence of metabolic compromise in the metastatic cancer population, is a risk factor for osteoporotic vertebral compression fractures in the general population and for mortality following spine surgery for metastatic disease. However, it is unknown whether sarcopenia can predict pathologic VCF after radiotherapy and improve fracture risk stratification. We hypothesize that sarcopenia is associated with earlier post-radiation pathologic VCF and shorter overall survival.

METHODS:

We conducted a retrospective study of 379 patients with spine metastases who were treated with radiotherapy at a tertiary care center from 2010 to 2021 and were not thought to be structurally unstable at the time of treatment, but subsequently experienced pathologic VCF requiring intervention (median follow-up was 15.1 months from the start of radiotherapy). Using digital CT segmentation, we estimated patients' Skeletal Muscle Index (SMI) scores, which were defined as the cross-sectional area of muscle at L3 normalized to height. We used a Kaplan-Meier analysis to compare overall survival and survival without fracture between patients with sarcopenia and those without, stratified by published sex-specific SMI thresholds for sarcopenia.

RESULTS:

Patients' demographic and tumor characteristics are detailed in Table 1. Fractures mostly commonly occurred at the thoracic (30%), thoracolumbar (30.5%), and lumbar (26.1%) regions. Thirty-four percent of males and 24% of females were sarcopenic ($p=0.032$). Patients with sarcopenia were more likely to receive conventional radiotherapy or lower dose SBRT ($p=0.035$). Eighty-four percent of patients underwent kyphoplasty; in 80% of cases, kyphoplasty was performed as a standalone procedure. Thirty-three percent of patients had surgery, and 56% of these procedures were entirely percutaneous. Fracture location and surgical treatment were not significantly different between patients with and without sarcopenia. Survival without fracture was shorter in patients with sarcopenia compared to those without (2.67 vs. 3.32 months), which was statistically significant on univariate ($p=0.0053$) and multivariate analysis ($p=0.019$) (Figure 1). Similarly, overall survival was shorter in patients with sarcopenia compared to those without (11.3 vs. 13.87 months), which was statistically significant on univariate ($p<0.0001$) and multivariate analysis ($p=0.014$) (Figure 2). Twenty-eight percent of patients with sarcopenia had a fracture within 1 month of radiotherapy, compared with 16% of those without sarcopenia ($p=0.015$).

DISCUSSION AND CONCLUSION:

In this cohort of patients who sustained pathologic VCF after radiotherapy, sarcopenia was significantly correlated with earlier fracture and reduced overall survival. Its additive discriminatory value for predictive models of pathologic VCF and overall survival should be further evaluated. As sarcopenia can be opportunistically diagnosed on regularly available cancer surveillance CT, it has the potential for widespread adoption to enhance fracture risk stratification and treatment making.

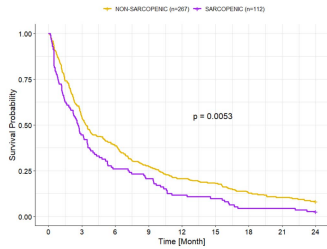


Figure 1. Kaplan-Meier analysis for survival without fracture by sarcopenia diagnosis

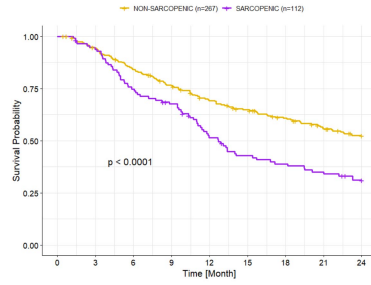


Figure 2. Kaplan-Meier analysis for overall survival by sarcopenia diagnosis

Table 1. Patient, Treatment, and Outcome Variables in Sarcopenic vs. Non-Sarcopenic Patients (N=379)

	Sarcopenic (N=112)	Non-Sarcopenic (N=267)	p value*
Age (years) [†]	64.60 ± 15.22	60.98 ± 11.81	0.026
Sex			0.032
Male	72 (64%)	139 (52%)	
Female	40 (36%)	128 (48%)	
Fracture Region			0.495
Cervical (C3-C6)	2 (2%)	4 (1%)	
Cervicodorsal (C7-T2)	2 (2%)	11 (4%)	
Thoracic (T3-T6)	36 (32%)	87 (33%)	
Thoracolumbar (T11-L1)	38 (34%)	87 (33%)	
Lumbar (L2-L4)	37 (33%)	70 (26%)	
Lumbosacral (L5)	7 (6%)	29 (11%)	
Radiotherapy Type			0.035
Conventional Radiotherapy	47 (42%)	83 (31%)	
Low-dose SBRT	10 (9%)	12 (4%)	
Mid-dose SBRT	35 (31%)	105 (39%)	
High-dose SBRT	20 (18%)	67 (25%)	
Intervention Type			0.836
Kyphoplasty	92 (82%)	225 (84%)	
Stadolone	73 (65%)	182 (68%)	
In Conjunction with Surgery	19 (17%)	43 (16%)	
Surgery	39 (35%)	85 (32%)	
Open	16 (14%)	38 (14%)	
Percutaneous	23 (21%)	47 (18%)	
Decompression	19 (17%)	52 (19%)	
Time to Fracture (months)			
< 1 month	31 (28%)	43 (16%)	0.015
1-3 months	30 (27%)	81 (30%)	0.062
3-6 months	21 (19%)	40 (15%)	0.362
≥ 6 months	30 (27%)	103 (39%)	0.018

* An independent two-samples t test was used for continuous variables that were normally distributed, the Mann-Whitney U test was used for non-normally distributed variables, and the chi-square or Fisher's exact test was used for categorical variables.
[†] Median was the selected measure of central tendency.