POSTER 69

Female Sex and Increased Number of Medical Comorbidities Associated with Increased Risk of Presenting with Pathological Femur Fracture in Metastatic Bone Disease

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Background: Many cancers metastasize to bone and may lead to pathologic fracture or impending pathologic fracture. Prophylactically stabilizing bones before fracture has been shown to be more cost-effective with improved outcomes. Many studies have examined risk factors for pathological fracture and identified radiographic findings and function pain as predominant indicators for surgery. These indicators are not all-encompassing nor are they associated with a strong predictive value. Common conditions that have been associated with poor bone health and increased risk of fracture in the non-oncologic population include diabetes mellitus, chronic obstructive pulmonary disease (COPD), cardiovascular disease, renal disease, smoking, corticosteroid use, and osteoporosis. However, these factors have not been studied in the context of metastatic bone disease. Thorough investigation of these factors could help providers identify candidates for prophylactic stabilization thereby reducing the number of completed pathological fractures.

Questions/purposes: Do known risk factors for poor bone health predispose cancer patients to pathologic fractures? Do medications such as bisphosphonates or antibodies to RANK-L affect the rates of pathological fracture in cancer patients?

Methods: 298 patients over the age of 40 with confirmed metastatic bone disease involving the femur and treated at an urban academic institution between 2010-2021 were retrospectively identified by CPT codes with expedited approval from an Institutional Review Board. Patients without complete medical documentation or with non-metastatic diagnoses were excluded. 193 patients met our inclusion and exclusion criteria, including 77 patients who presented with completed pathological femur fractures and 116 patients who presented for prophylactically stabilization due to high risk of fracture, as judged by the treating surgeon. Patient demographics, age at surgery, date of surgery, and cancer histology were collected. Clinical diagnoses including diabetes mellitus, COPD, cardiovascular disease, osteoporosis, active tobacco or corticosteroid use, and end-stage renal disease (ESRD; CKD Stage IV, GFR< 15ml/min, or use of hemodialysis) that were current within three months pre-operatively were considered comorbidities and recorded. Bisphosphonate RANK-L inhibitor use within three months of preoperatively was also recorded. Using anesthesia records from the date of service, patient weight and height were also collected. Descriptive statistics were compiled with univariate analysis by Mann-Whitney or chi-squared testing. A multiple logistic regression analysis was performed after stepwise backward selection to identify the most significant patient variables for presenting with completed fracture.

Results: Descriptive statistics on comorbidity and medication use between groups is shown in **Table 1**. On univariate analysis, patients with COPD were more likely to present with pathologic fracture (20/33 [61%] compared to 57/160 [36%], p = 0.01), as were patients with an increasing number of comorbidities overall (30/59 [51%] for 2+ comorbidities compared to 18/62 [29%] with 0 comorbidities, p < 0.05). On multivariable logistic regression analysis (**Figure 1**), patients with female sex (odds ratio [OR]: 1.84; p=0.046) or 2 or more comorbidities (OR: 2.60; p=0.02) were more likely to present with a completed femur fracture. Bisphosphonate use was associated with a lower likelihood of presenting with a pathological fracture but did not reach statistical significance (OR: 0.18; p=0.120).

Conclusions: We present a retrospective investigation to determine whether known risk fractures for poor bone health and non-oncologic fracture are also associated with patients who present with a completed pathologic femur fracture, compared to those patients who present for prophylactic fixation of an impending femur fracture. This analysis suggests that females and those with an increasing number of comorbidities may be at increased risk for pathologic fracture. Several trends were noted with specific comorbidities and antiresorptive therapies, but this

analysis was likely underpowered to evaluate this comprehensively. Further, we did not account for socioeconomic differences that may predispose to both comorbidities and access to care before fracture. Despite these limitations, this study raises the possibility that patient factors and/or comorbidities alter bone strength and/or pain experiences that may mislead orthopaedic oncologists weighing prophylactic stabilization of femur lesions in the setting of metastatic bone disease. Future studies are needed using larger patient cohorts to adequately address this question.

Level of evidence: Retrospective case-control study, Level III evidence

Table 1. Preoperative characteristics and comorbidities in patients presenting for prophylactic stabilization of impending pathologic fractures, compared to those presenting with completed pathologic fracture. p-value less than 0.05 is significant.

	Prophylactic Stabilization (N=116)	Completed Fracture (N=77)	p value
Age (years)			
Mean (SD)	64.8 (10.6)	65.3 (12.1)	0.68
Sex			
Male	63 (66.3%)	32 (33.7%)	0.11
Female	53 (54.1%)	45 (45.9%)	
Body mass index (BMI)			
Mean (SD)	30.3 (15.4)	30.2 (8.87)	0.57
Chronic obstructive pulmonary disease (COPD)			
No	103 (64.4%)	57 (35.6%)	**0.01**
Yes	13 (39.4%)	20 (60.6%)	
Smoker			
No	89 (59.3%)	61 (40.7%)	0.82
Yes	27 (62.8%)	16 (37.2%)	
Cardiovascular disease			
No	95 (62.5%)	57 (37.5%)	0.26
Yes	21 (51.2%)	20 (48.8%)	
Diabetes			
No	90 (62.5%)	54 (37.5%)	0.32
Yes	26 (53.1%)	23 (46.9%)	

	Prophylactic Stabilization (N=116)	Completed Fracture (N=77)	p value
End stage renal disease (ESRD)			
No	114 (61.0%)	73 (39.0%)	0.22
Yes	2 (33.3%)	4 (66.7%)	
Osteoporosis			
No	114 (60.7%)	74 (39.3%)	0.39
Yes	2 (40.0%)	3 (60.0%)	
Steroid use			
No	94 (62.3%)	57 (37.7%)	0.33
Yes	22 (52.4%)	20 (47.6%)	
Number of comorbidities			
0	44 (71.0%)	18 (29.0%)	**0.0496**
1	43 (59.7%)	29 (40.3%)	
2+	29 (49.2%)	30 (50.8%)	
Bisphosphonate use			
No	108 (58.7%)	76 (41.3%)	0.09
Yes	8 (88.9%)	1 (11.1%)	
Denosumab use			
No	115 (59.9%)	77 (40.1%)	1.00
Yes	1 (100%)	0 (0%)	

Variable	Odds ratio	95% CI		p value
Sex				
Male	Ref			
Female	1.84	1.01–3.40		0.046
Number of comorbidities				
0	Ref			
1	1.81	0.87–3.85		0.116
2 or more	2.60	1.22–5.68		0.015
Bisphosphonates				
No	Ref			
Yes	0.18	0.01–1.08		0.120

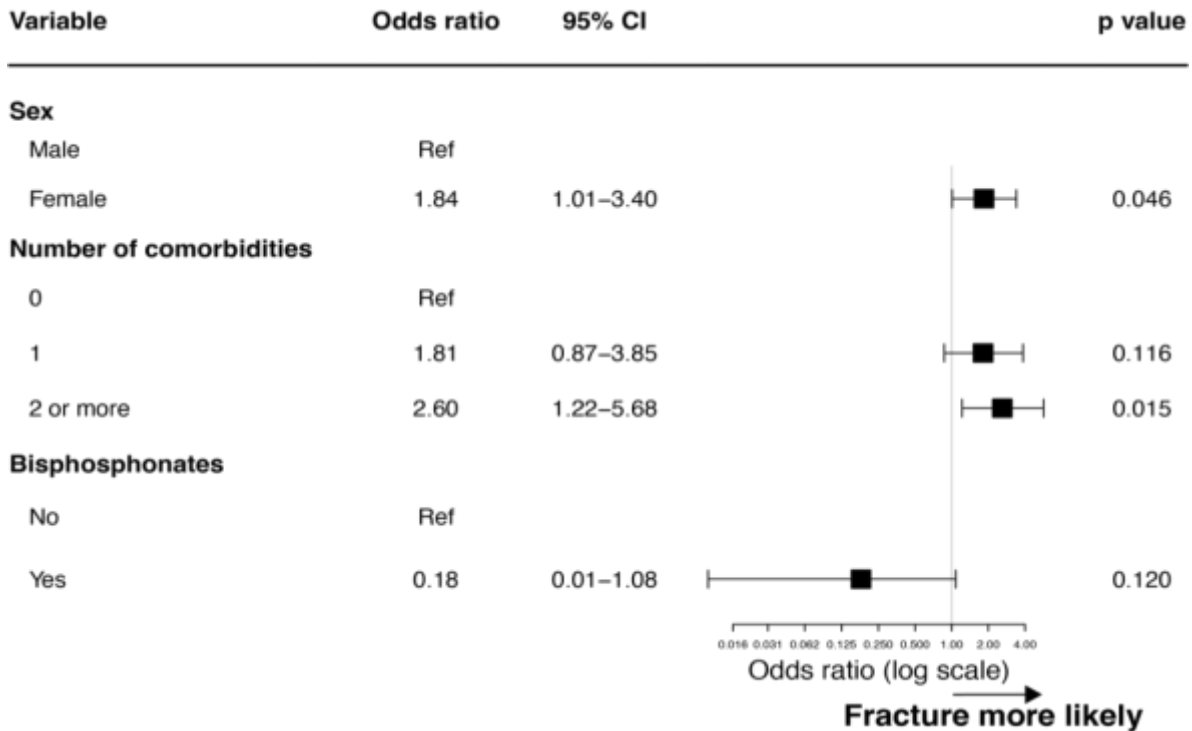Odds ratio (log scale) — **Fracture more likely**

Figure 1. Logistic regression analysis after stepwise backward selection of factors associated with fracture on presentation. Unstandardized odds ratios are displayed on a logarithmic scale with 95% confidence intervals. CI indicates confidence interval. p-value less than 0.05 is significant.