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Research Paper

The low and disproportionate utilization of antiresorptive therapy in patients with osseous metastasis

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HIGHLIGHTS

- Only 7.7 % of patients with osseous metastases are prescribed antiresorptive therapy.
- 7.3 % of patients with osseous metastases sustain a pathologic fracture.
- Younger and male patients are less likely to receive treatment.

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ABSTRACT

Introduction: Antiresorptive therapies are commonly utilized to mitigate and prevent skeletal-related-events in patients with metastatic osseous disease. However, limited data exists on the incidence or factors associated with prescription of antiresorptives or their effects on the incidence of pathologic fractures in patients with osseous metastatic disease. The aims of this study were to determine 1) the proportion of patients with osseous metastasis who receive antiresorptive therapy and sustain a pathologic fracture within 2-years of a new diagnosis, 2) factors associated with sustaining a pathologic fracture, and 3) factors are associated with the likelihood of receiving antiresorptive therapy.

Methods: Between January 2010 and October 2021, 1,492,301 patients with a new diagnosis of osseous metastasis were captured in the Mariner dataset of the PearlDiver database. Patients were identified using International Classification of Disease (ICD) 10 codes for osseous metastasis. We excluded patients with a prior diagnosis of osseous metastasis and if they had less than two-years of follow-up. There were 696,459 patients (46.7 %) included for analysis. Of these patients, 63 % (N = 437,716) were over the age of 65, 46 % were women, and 5.6 % had Medicaid insurance. We identified patients who were prescribed antiresorptive therapy within 2-years of a new diagnosis of osseous metastasis. Cox proportional hazard ratio models were created to predict factors associated with 1) pathologic fracture and 2) receiving antiresorptive therapy within 2-years of a new diagnosis of osseous metastasis, respectively.

Results: The incidence of antiresorptive therapy prescription was 7.7 % in our cohort. The incidence of pathologic fracture within 2-years of a new diagnosis was 7.3 %. The risk of sustaining a pathologic fracture was higher for patients aged 35–44 (HR 1.27 [95 % CI 1.08–1.51]; $p = 0.004$), those with primary kidney cancer (HR 1.78 [95 % CI 1.71–1.85]; $p < 0.001$), $p = 0.005$), multiple myeloma (HR 2.49 [95 % CI 2.39–2.59]; $p < 0.001$), and Medicaid insurance (HR 1.17 [95 % CI 1.13–1.21]; $p < 0.001$). The risk of sustaining a pathologic fracture was lower for patients on antiresorptive therapy (HR 0.71 [95 % CI 0.66–0.83]; $p < 0.001$). Increasing age was an independent predictor for antiresorptive therapy prescription (HR 1.77–16.38, all $p < 0.05$). Male sex as well as diagnosis of primary prostate, lung, or kidney cancer and Medicaid insurance were negative predictors for antiresorptive prescription (HR 0.15–0.87, all $p < 0.001$).

Conclusions: The utilization of antiresorptive therapy in patients with osseous metastases remains unacceptably low, with only 7.7% patients being prescribed these therapies, despite shown efficacy in reduction of pathologic fractures incidences. This study identified younger patients, males, and those diagnosed with primary prostate,

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kidney, and lung cancers to be at increased risk of not being prescribed antiresorptive therapy, suggesting possible bias in prescription patterns. Greater efforts are needed by providers who care for this vulnerable population to increase the utilization and reduce disparities of prescribing antiresorptive therapy.

1. Introduction

Due to increased lifespan as well as improved detection, surveillance, and chemotherapy/immunotherapy regimens, the prevalence of cancer in the United States continues to increase, with a projected 24 % increase in patients living with cancer by 2032 [1,2]. While metastatic disease portends a poor prognosis, osseous metastases have an increased risk of morbidity and mortality due to skeletal-related-events (SRE) [3]. SREs are defined as pathologic fractures, spinal cord compression, bone pain, as well as the subsequent treatment of metastases with radiation and/or surgical intervention [3,4]. Current treatment paradigms in mitigating and preventing SREs include the prescription of antiresorptive therapies, such as bisphosphonates and denosumab. [5,6]. Antiresorptive therapies act by inhibiting osteoclast activation by tumor cells, preventing a negative bone balance that may induce a fracture. Additional research suggests antiresorptive therapies may prevent progression of disease by reducing bone-derived growth factors required for tumoral growth and propagation [5].

Thus, the utilization of antiresorptives is paramount to reduce SREs in patients with metastatic bone disease. However, limited literature exists regarding the utilization of antiresorptive prescriptions, its risk reduction for SREs in varying primary cancers, and the existence of prescription biases in this at-risk population. Recent orthopaedic trauma and spine literature has documented low rates of antiresorptive prescriptions in patients who sustained fragility fractures [7,8]. Barton et al [7] retrospectively analyzed patients 50 years old or greater with new vertebral compression fractures and found only 12 % of patients initiated antiresorptive therapy within 1-year of fracture with 38 % of patients sustaining a second fragility fracture within 2-years. Bogoch et al [8] also illustrated low rates of antiresorptive therapies, with only 25 % of patients following fragility hip fractures receiving these therapies. While the significant treatment gap is well established in the osteoporosis population, the utilization of these therapies in patients with osseous metastasis is unknown.

Herein, our primary objectives were to determine the proportion of patients with osseous metastases who receive antiresorptive therapy and the proportion of patients who sustain a pathologic fracture within 2-years of osseous metastasis diagnosis. Our secondary objectives were to assess factors associated with receiving antiresorptive therapy within 2-years of osseous metastasis diagnosis, as well as factors associated with sustaining a pathologic fracture within 2-years of new diagnosis.

2. Material and methods

2.1. Study design and setting

A retrospective, comparative analysis was conducted using the Mariner dataset of PearlDiver Patient Records Database (https://www.pearldiverinc.com). This dataset contains patient all-payer claims information of over 150 million patients from January 2010 to October 2021 in the United States.

2.2. Patients

Between January 2010 and October 2021, 1,492,301 patients with a diagnosis of osseous metastasis were captured in the Mariner dataset. Patients were identified using International Classification of Disease (ICD) 9/10 diagnosis codes (Appendix 1). Only patients with an ICD-10 code for osseous metastasis were included as ICD-10 codes clearly define the location of pathologic fracture for subsequent analysis. As ICD-10 codes were initiated in October 2015, only patients with a diagnosis of osseous metastasis from October 2015 to October 2021 were included. We isolated patients with a new diagnosis of osseous metastasis from patients with a prior diagnosis of osseous metastasis by using both ICD-9 and 10 codes to exclude patients with a prior diagnosis within one-year before the observed diagnosis. Following this initial criteria, 54.7 % (816,314 of 1,492,301) of patients with a new diagnosis of osseous metastasis were eligible. Only patients with at least 2-year follow-up after a new diagnosis of osseous metastasis were included, excluding 15 % (119,855 of 816,314) of patients due to loss to follow-up, incomplete datasets, or mortality.

2.3. Descriptive data

In total, 696,459 patients were included. Sixty-three percent (N = 437,716) of patients with a diagnosis of osseous metastasis were over the age of 65 and 46 % (N = 322,638) were women. Fifty-four percent (N = 381,033) had commercial insurance, 30 % (N = 208,123) had Medicare insurance, 5.6 % (N = 38,838) had Medicaid insurance, and 9.7 % (N = 67,710) had non-Commercial/Medicare insurance. The most common cancer types were: prostate cancer (24 %, N = 166,697), lung cancer (23 %, N = 160,229), breast cancer (20 %, N = 141,413), kidney cancer (5.9 %, N = 41,324), multiple myeloma (5.7 %, N = 39,971), lymphoma (4.5 %, N = 31,427), and unknown/unreported (15 %, N = 104,447) (Table 1).

2.4. Primary outcome

The primary outcomes were defined as utilization rate of antiresorptive medications and incidence rate of pathologic fracture within 2-years following a new diagnosis of osseous metastasis. Antiresorptive

Table 1
Patient characteristics of patients with osseous metastasis (**N = 696,459**).

Parameter	Osseous Metastasis
Age	
<25	0.3 (2,143)
25–34	1.0 (7,081)
35–44	3.1 (21,506)
45–54	9.2 (63,768)
55–64	23.6 (164,245)
65–74	30.6 (213,079)
75+	32.2 (224,637)
Women	46.3 (322,638)
Primary Cancer Type	
Breast	20.3 (141,413)
Prostate	23.9 (166,697)
Kidney	5.9 (41,324)
Lung	23.0 (160,229)
Lymphoma	4.5 (31,427)
Multiple Myeloma	5.7 (39,971)
Thyroid	1.6 (10,921)
Other	15.0 (104,477)
Antiresorptives	7.7 (53,258)
Insurance Type	
Commercial	54.7 (381,033)
Medicare	29.9 (208,123)
Medicaid	5.6 (38,838)
Other	9.7 (67,710)

Data presented as % (n).

medications included bisphosphonates and denosumab formulations that were defined using generic and brand name drug codes (Appendix 1). Pathologic fractures (shoulder, humerus, ulna, radius, hand, pelvis, femur, tibia, fibula, ankle, foot, and other) were defined using ICD-10 diagnosis codes (Appendix 1) (see Table 2).

2.5. Secondary outcomes

Secondary outcomes included an evaluation of factors associated with sustaining a pathologic fracture and receiving antiresorptive medications within 2-years of the first diagnosis of osseous metastasis. To observe factors associated with receiving antiresorptive medication within 2-years, key variables included age (<25, 25–34, 35–44, 45–54, 55–64, 65–74, and 75+), sex (men or women), primary cancer type (breast, prostate, kidney, lung, lymphoma, multiple myeloma, thyroid, and other), and insurance type (commercial, Medicare, Medicaid, other) (Appendix 1). To observe factors associated with sustaining a pathologic fracture, key variables included age (<25, 25–34, 35–44, 45–54, 55–64, 65–74, and 75+), sex (men or women), primary cancer type (breast, prostate, kidney, lung, lymphoma, multiple myeloma, thyroid, and other), insurance type (commercial, Medicare, Medicaid, other), and the utilization of a prior antiresorptive medication (Appendix 1).

2.6. Ethical approval

As PearlDiver only releases de-identified information to users, this study was exempt from institutional review board approval.

Table 2
Factors Associated with Pathologic Fracture in Patients with Osseous Metastasis.

	% (n)[†]	HR (95 % CI)	P-value
Incidence of pathologic fracture	7.3 (51,006)[‡]	–	–
Age			
<25	0.3 (163)	REF	REF
25–34	1.2 (614)	1.14 (0.95–1.37)	0.158
35–44	4.1 (2,092)	1.27 (1.08–1.51)	**0.004**
45–54	11.3 (5,775)	1.15 (0.98–1.36)	0.089
55–64	28.0 (14,298)	1.13 (0.97–1.33)	0.134
65–74	30.2 (15,403)	1.01 (0.86–1.19)	0.932
75+	24.8 (12,661)	0.84 (0.71–0.99)	**0.029**
Sex			
Women	50.9 (25,983)	REF	REF
Men	49.1 (25,023)	0.92 (0.90–0.94)	**<0.001**
Primary Cancer Type			
Breast	20.1 (10,229)	REF	**REF**
Prostate	15.0 (7,648)	0.64 (0.61–0.66)	**<0.001**
Kidney	9.6 (4,914)	1.78 (1.71–1.85)	**<0.001**
Lung	24.1 (12,298)	1.04 (1.01–1.08)	0.058
Lymphoma	4.7 (2,377)	0.93 (0.89–0.98)	**0.005**
Multiple Myeloma	12.5 (6,393)	2.49 (2.39–2.59)	**<0.001**
Thyroid	1.8 (911)	1.06 (0.98–1.14)	0.151
Other	12.2 (6,236)	0.93 (0.89–0.97)	**<0.001**
Prior Antiresorptive	4.2 (2,151)	0.71 (0.66–0.83)	**<0.001**
Insurance Type			
Commercial	58.1 (29,618)	REF	REF
Medicare	24.8 (12,634)	0.86 (0.84–0.88)	<0.001
Medicaid	7.4 (3,754)	1.17 (1.13–1.21)	<0.001
Other	9.7 (4,922)	0.77 (0.72–0.82)	<0.001

[†]For this category, percentages were calculated from the total number of patients who received antiresorptive therapy, not the entire number of patients included in this study; [‡]The total number of patients included in the study was used to calculate this specific incidence.

2.7. Statistical analysis

We evaluated the prescription incidence of antiresorptive medication within 2-years following a new diagnosis of osseous metastasis by dividing the number of patients with a new diagnosis of osseous metastasis prescribed an antiresorptive medications within 2-years of a new diagnosis by the total number of patients with a new diagnosis of osseous metastasis. We calculated the incidence rate of pathologic fracture by dividing the number of patients with a new diagnosis of osseous metastasis that sustained a pathologic fracture within 2-years of diagnosis by the total number of patients with a new diagnosis of osseous metastasis. We estimated two separate Cox proportional hazard models to identify key variables associated with the odds of 1) sustaining a pathologic fracture and 2) being prescribed an antiresorptive medication within 2-years of a new diagnosis of osseous metastasis. Statistical analysis was conducted using R software (R Foundation for Statistical Computing) provided by the PearlDiver database.

3. Results

3.1. Incidence of two-year antiresorptive prescription and pathologic fracture in patients with new osseous metastasis

A total of 7.7 % (53,258 of 696,459) of patients with a new diagnosis of osseous metastasis were prescribed an antiresorptive treatment within 2-years following a new diagnosis. The median time from a new diagnosis of osseous metastases to antiresorptive therapy was 84 days (interquartile range 25 to 360 days). A total of 7.3 % (51,006 of 696,459) sustained a pathologic fracture within 2-years following a new diagnosis. The median time from a new diagnosis of osseous metastases to pathologic fracture was 283 days (interquartile range 102 to 541 days). Of those with a pathologic fracture, 4.2 % were prescribed an antiresorptive treatment prior to pathologic fracture.

3.2. Factors associated with pathologic fracture in patients with new osseous metastasis

The risk of sustaining a pathologic fracture within 2-years following a new diagnosis of osseous metastasis was higher in patients aged 35–44 (HR 1.27 [95 % CI 1.08–1.51]; $p = 0.004$), those with primary kidney cancer (HR 1.78 [95 % CI 1.71–1.85]; $p < 0.001$), multiple myeloma (HR 2.49 [95 % CI 2.39–2.59]; $p < 0.001$), and those with Medicaid insurance (HR 1.17 [95 % CI 1.13–1.21]; $p < 0.001$). The risk of sustaining a pathologic fracture within 2-years following a new diagnosis of osseous metastasis was lower in patients aged 75+ (HR 0.84 [95 % CI 0.71–0.99]; $p = 0.029$), men (HR 0.92 [95 % CI 0.90–0.94]; $p < 0.001$), those with primary prostate cancer (HR 0.64 [95 % CI 0.61–0.66]; $p < 0.001$), primary lymphoma (HR 0.93 [95 % CI 0.89–0.98]; $p = 0.005$), prescribed an antiresorptive medication before fracture (HR 0.71 [95 % CI 0.66–0.83]; $p < 0.001$), Medicare insurance (HR 0.86 [95 % CI 0.84–0.88]; $p < 0.001$) and non-Commercial/Medicare insurance (HR 0.77 [95 % CI 0.72–0.82]; $p < 0.001$).

3.3. Factors associated with patients with new osseous metastasis being prescribed antiresorptive medication

The risk of being prescribed an antiresorptive medication were higher in those aged 35–44 (HR 1.77 [95 % CI 1.09–3.11]; $p = 0.031$), aged 45–54 (HR 3.01 [95 % CI 1.87–5.25]; $p < 0.001$), aged 55–64 (HR 6.43 [95 % CI 4.01–11.21]; $p < 0.001$), aged 65–74 (HR 11.93 [95 % CI 7.45–20.79]; $p < 0.001$), and 75+ (HR 16.38 [95 % CI 10.22–28.54]; $p < 0.001$). The risk of being prescribed an antiresorptive medication were lower in men (HR 0.15 [95 % CI 0.15–0.16]; $p < 0.001$), those with primary prostate cancer (HR 0.34 [95 % CI 0.32–0.36; $p < 0.001$), primary kidney cancer (HR 0.39 [95 % CI 0.27–0.41]; $p < 0.001$), primary lung cancer (HR 0.68 [95 % CI 0.66–0.71]; $p < 0.001$), primary

lymphoma (HR 0.69 [95 % CI 0.48–0.74]; p < 0.001), multiple myeloma (HR 0.71 [95 % CI 0.62–0.79]; p < 0.001), primary thyroid cancer (HR 0.77 [95 % CI 0.60–0.83]; p < 0.001), Medicaid insurance (HR 0.87 [95 % CI 0.83–0.92]; p < 0.001), Medicare insurance (HR 0.94 [95 % CI 0.92–0.96]; p < 0.001), and non-Commercial/Medicare insurance (HR 0.86 [95 % CI 0.81–0.91]; p < 0.001) (Table 3).

4. Discussion

The presence of skeletal-related-events is associated with increased patient morbidity and mortality, as only 30 % of patients survive 12 months after sustaining a pathologic fracture [9]. Antiresorptive therapies have been proven to reduce the risk of SREs and improve overall bone health in patients with osseous metastases in various cancers [10]. Thus, the metastatic bone disease population would be expected to be prescribed antiresorptive therapies with high frequencies. Unfortunately, there is limited literature on the utilization and factors associated with antiresorptive therapy prescriptions in patients with metastatic cancer, especially in the United States.

Our study identified that only 7.7 % of patients with osseous metastases were prescribed antiresorptive therapy. We additionally identified a rate of pathologic fracture of 7.3 % within 2-years of osseous metastasis diagnosis. Female sex, increasing age, and breast cancer were factors more likely to be associated with prescription of antiresorptive therapy. Younger patients and those with primary kidney cancer or multiple myeloma were more likely to sustain a pathologic fracture. Additionally, those who were prescribed antiresorptive therapies had a significantly reduced risk of sustaining pathologic fracture. This study suggests a substantial gap in oncologic care and potential bias for antiresorptive prescriptions in patients with osseous metastases.

Table 3
Factors associated with antiresorptive treatment in patients with osseous metastasis.

Category	% (n)[†]	HR (95 % CI)	P-value
Incidence of antiresorptive prescription	7.7 (53,258)[‡]	–	–
Age			
<25	0.03 (15)	REF	REF
25–34	0.2 (82)	1.17 (0.69–2.11)	0.587
35–44	0.8 (418)	1.77 (1.09–3.11)	**0.031**
45–54	3.6 (1,892)	3.01 (1.87–5.25)	**<0.001**
55–64	16.5 (8,803)	6.43 (4.01–11.21)	**<0.001**
65–74	34.4 (18,337)	11.93 (7.45–20.79)	**<0.001**
75+	44.5 (23,711)	16.38 (10.22–28.54)	**<0.001**
Sex			
Women	75.7 (40,308)	REF	REF
Men	24.3 (12,950)	0.15 (0.15–0.16)	**<0.001**
Primary Cancer Type			
Breast	32.8 (17,451)	REF	REF
Prostate	16.1 (8,570)	0.34 (0.32–0.36)	**<0.001**
Kidney	4.1 (2,183)	0.39 (0.27–0.41)	**<0.001**
Lung	24.8 (13,225)	0.68 (0.66–0.71)	**<0.001**
Lymphoma	4.9 (2,619)	0.69 (0.48–0.74)	**<0.001**
Multiple Myeloma	6.4 (3,406)	0.71 (0.62–0.79)	**<0.001**
Thyroid	1.9 (1,033)	0.77 (0.60–0.83)	**<0.001**
Other	9.0 (4,771)	0.23 (0.19–0.26)	**<0.001**
Insurance Type			
Commercial	52.0 (27,663)	REF	REF
Medicare	35.7 (19,016)	0.94 (0.92–0.96)	**<0.001**
Medicaid	3.5 (1,849)	0.87 (0.83–0.92)	**<0.001**
Other	8.8 (4,692)	0.86 (0.81–0.91)	**<0.001**

[†]For this category, percentages were calculated from the total number of patients who received antiresorptive therapy, not the entire number of patients included in this study; [‡]The total number of patients included in the study was used to calculate this specific incidence.

4.1. Limitations

Due to utilization of an administrative claims database, we are limited to both the reliability and limited information provided by these billing codes. We are unable to discern the primary cancer type for 15 % of patients and fracture location for 46 % of patients who sustained a pathologic fracture. We believe that most unknown fractures may be of the spine, as there are no specific codes for pathologic spine fractures. Additionally, the billing codes are not granular enough to parse out if patients presented with multiple sites of osseous metastases. It should be noted we did not analyze all types of SRE and focused only on pathologic fractures, which underrepresents the number and spectrum of SREs, such as hypercalcemia or spinal cord compression. However, the limited data for specific fracture location does not take away from the primary findings of a low overall utilization of antiresorptive medications, disparities associated with prescription, and the risk reduction of pathologic fracture when receiving antiresorptive treatment. Second, we do not have data on disease severity and patient symptoms/functional status that may impact decision-making for receiving treatments. Third, we utilized insurance type as a surrogate for social determinants of health. However, our administrative claims database is not generalizable to the uninsured population. Additionally, our dataset lacks racial information. Race has previously shown to impact access and quality of care. Future studies can show the interplay of race on access to antiresorptive medications as well as use other surrogates for social determinants of health, such as the area of deprivation index. Nonetheless, this is the first study to show disparities in access to treatment based on age, sex, primary cancer type, and insurance type. Finally, although the database contains patient records of over 150 million patients, this study is likely not generalizable to treatment of uninsured patients or those in other countries.

5. Two-Year antiresorptive medication prescription and pathologic fracture rates in patients with osseous metastasis

Despite the clinical efficacy of denosumab and bisphosphonates in reducing SREs, our study demonstrates a low rate of antiresorptive therapy initiation in patients with osseous metastases. We found the rate of antiresorptive therapy prescription within 2-years of new diagnosis of osseous metastasis, was 7.7 % in our cohort. Additionally, the incidence of pathologic fracture, within 2-years of new diagnosis of osseous metastasis was 7.3 % in our cohort, which is similar to prior literature [11,12]. There is no prior literature documenting the incidence of antiresorptive therapy prescriptions in patients with osseous metastases of varying cancers in the United States to these authors' knowledge; however, this study clearly indicates a bias in the treatment of women and those with breast cancer with anti-resorptive therapy above other cancer types. This may perhaps be secondary to prior publication bias in the breast cancer literature as well as the training of breast oncologists in the prescription of these medications, given the additional association of estrogen with bone turnover. There is retrospective literature from Germany that analyzed breast cancer patients and found 20.2 % were prescribed antiresorptives within 5-years of initiating endocrine therapies [13].

We are unable to determine why antiresorptive therapies were not routinely prescribed in our cohort, but we hypothesize both patient and provider factors. First, there is no precedent on which provider (medical

oncology, orthopaedic oncology, or primary care) prescribes antiresorptive therapies. Therefore, the lack of communication or ownership of prescription may lead to decreased rates of overall antiresorptive therapy initiation. Second, while antiresorptive therapies are generally well-tolerated, there are rare complications such as osteonecrosis of the jaw. Thus, most patients require dental clearance prior to initiation of antiresorptive therapy, which may lead to delay or limitations in prescription [14]. Further education on antiresorptive therapies and their significance in reducing the risk of SREs and promotion of bone health is required in both orthopaedic surgeons and medical oncologists. Additionally, we suggest creation of an antiresorptive task force within surgical oncology and medical oncology to improve screening, prescription, and overall care for this at-risk population.

6. Factors associated with pathologic fracture in patients with osseous metastasis

In the current study, patients who were younger, diagnosed with primary kidney cancer or multiple myeloma, and had Medicaid insurance were at an increased risk for sustaining pathologic fractures. In contrast, patients with breast cancer and use of antiresorptive therapies were negative predictors for sustaining pathologic fractures. Specifically, we found antiresorptive therapies reduced the risk of pathologic fractures by 29 %, which is comparable to prior randomized control trial results [6,10,15].

Pathologic fracture prediction and prevention is a constant topic of interest in orthopaedic oncology, as completed fractures have associated increased patient morbidity and decreased survival. Mosher et al [16] assessed outcomes in patients with pathologic fractures and found patients who sustained pathologic fractures were younger, female, had non-commercial insurance, increased blood transfusions, length of stay/hospitalization, total cost of care, and in-hospital mortality compared to patients who underwent prophylactic fixation for osseous metastases, similar to our results. Contrary to our study, literature has identified patients with breast cancer to be at increased risk of pathologic fracture, likely due to a prolonged survival time compared to other tumors[17]. We hypothesize our study did not observe an increased risk due to the increased proportion of breast cancer patients receiving antiresorptive therapy and possibly duration of follow-up. We additionally hypothesize that younger patients may be at increased fracture risk, given that many metastatic diseases are now treated as chronic disease. These patients, thus, may lead more active, high demand lifestyles. Ultimately, we believe further research in developing risk stratification tools that specifically utilize at-risk demographics (patient age, sex, and tumor biology), to identify patients at risk for pathologic fractures is required.

7. Factors associated with patients with osseous metastasis being prescribed antiresorptive medication

We identified younger patients, males, those with non-commerical insurance, and primary kidney, lung, and prostate cancer were at increased risk of not receiving antiresorptive therapy within 2 years of osseous metastasis diagnosis. Interestingly, the odds of receiving antiresorptive therapy increased significantly in each age cohort, with those aged 75-years or older having 16.3 times greater odds of being prescribed antiresorptive therapies. We hypothesize this is due to providers associating the requirement for bone health in older patients who are likely osteopenic or osteoporotic, in addition to having osseous metastases. It should be emphasized men were 6.7 times less likely to be prescribed antiresorptive therapies. This may be due to an unconscious bias of bisphosphonates being used for women with poor bone health, as previous literature in geriatric fragility fractures demonstrated men are less likely to be prescribed antiresorptive therapy [18]. Another bias may be due to prostate cancer being the most common cancer in men, which produces predominantly sclerotic metastases and are less likely than other cancers to present with hypercalcemia of malignancy[19]. Despite this, prostate tumor cells promote osteolytic processes within metastases and benefit from antiresorptive therapy. Literature has shown decreased SRE rates with initiation in this cohort, including patients with sclerotic, castrate-resistant prostate cancer [20]. A similar selection bias may exist in patients with primary kidney cancer, as some of these patients present with oligometastatic disease and undergo wide excision of the lesion, which has been documented to confer a survival benefit and possible cure [21]. Nonetheless, antiresorptive use has demonstrated SRE reductions in this cohort [22]. In contrary to our results, which originates from the United States, an Italian survey of oncologists reported 83 % of their 61,064 patients with osseous metastases received antiresorptive therapy[23]. The disparity of antiresorptive prescription between our study and the Italian oncologist survey is beyond the scope of this analysis. These authors hypothesize it is multifactorial but could include differences in overall delivery of health care (universal public vs largely private) and ownership of prescription practices. To the authors' knowledge, this is the first study assessing predictors associated with antiresorptive prescription in the United States for patients with varying solid tumors and osseous metastases. Further research assessing biases in prescription patterns of antiresorptives are required, as well as continued education on their benefits in most osseous metastatic disease patients.

8. Conclusion

Prescription of antiresorptive therapy in patients with osseous metastases is unacceptably low despite proven efficacy in reducing skeletal-related-events, long term tolerance in patients, and possible reduction progression of disease in certain cancers. Prescription of antiresorptive therapy within 2 years of new diagnosis reduced the risk of pathologic fracture by 29 %, while younger patients with primary kidney cancer and multiple myeloma were at increased risk for pathologic fracture. This study identified younger patients, males, those diagnosed with primary prostate, kidney, and lung cancers, and those with noncommercial insurance to be at increased risk of not being prescribed antiresorptive therapy, suggesting possible bias in prescription patterns. Greater efforts are needed by providers who care for this vulnerable population to increase the utilization and reduce disparities of prescribing antiresorptive therapies.

CRediT authorship contribution statement

Amil R. Agarwal: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Christa L. LiBrizzi:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Lauren Wessel:** Investigation, Writing – original draft, Writing – review & editing. **Savyasachi C. Thakkar:** Conceptualization, Software, Validation, Resources, Investigation, Writing – review & editing, Supervision. **Adam S. Levin:** Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbo.2023.100507.

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