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Abstract

INTRODUCTION: Higher versus lower total number of fracture risk factors has been linked to increased fracture risk among postmenopausal patients. This study characterized the risk of vertebral fracture (VF) associated with specific combinations of fracture risk factors (RFs) among postmenopausal patients with a diagnosis of osteopenia, osteoporosis, or who had used osteoporosis therapies.

METHODS: In this observational cohort study we used electronic medical record (EMR) data to identify patients treated by primary care clinicians from 1995-2005 who met inclusion criteria. Primary RFs of interest identified in a 390 day run-in period were age, body mass index (BMI), bone mineral density (BMD), fracture since age 50, and maternal fracture or osteoporosis history. Other RFs including patient-specific characteristics, drug exposures, and comorbid diseases were also evaluated. Cox Proportional Hazards models were used to estimate the risk of VF over time for each RF in univariate and multivariable models. Risks for patients with specific combinations of RFs were calculated.

RESULTS: A total of 50,783 patients were identified with a mean age of 66.8 (SD 8.6). Race was identified for 15,679 (30.9%); 82.8% were Caucasian. BMD T-scores were present in 3,431 (6.8%); 52.4% had T-scores in the osteopenia and 25.9% in the osteoporosis ranges. BMI was available for 42,446 (83.6%) of patients; 22.0% were obese or extremely obese (BMI ≥30), 33.8% were overweight (BMI from 25-29.9), 41.4% were normal weight (BMI from 18.5-24.9), and 2.8% were underweight (BMI<18.5). A prior fracture since age 50 was identified in 1,769 (3.5%); 1.5% (742) had a prior VF and 0.7% (374) had a prior hip fracture. Maternal history of fracture was not available. Incident VFs occurred in 627 patients (1.2%) after a mean of 25.3 months. In the univariate analyses, increasing age, decreasing BMI, a prior fracture since age 50, and race were statistically significant predictors of VF. BMD was not a significant predictor in this patient sample, though we could not rule out the interference of other factors. In the multivariable models, decreasing BMI was not significant, of the primary RFs, only age and prior fracture were used. Combined hazards for VF were substantially higher for older patients with prior fractures, as shown in Figure 1.

CONCLUSIONS: The risk for VF increased with age in each 5-year increment and was statistically significant by age 65 versus 50-54. The risk was increased with both prior VF and prior non-VF and was from 5-19 times higher, depending on prior fracture type and age.

Background

- Fractures are the most significant clinical and economic manifestation of osteoporosis
- The incidence of vertebral fracture (VF) in women with postmenopausal osteoporosis (PMO) has been shown to increase with age, doubling for women 65 and older versus women aged 50-64¹
- The risk of fracture increases as the number of independent risk factors increases, yet the importance of specific combinations of risk factors for predicting subsequent fractures has not yet been determined in a real-world setting

Objectives

1. Model the risk of vertebral fracture (VF) associated with five clinical risk factors for fracture among PMO patients in a national electronic medical record dataset, adjusting for disease and treatment covariates
2. Calculate the increased risk of VF for patients with specific combinations of clinical risk factors

Methods

Data source

- GE Centricity™ database is a commercially-available electronic medical record (EMR) that contains electronic longitudinal clinical patient data for about 3.7 million patients in primary care clinics from 1995-2005

Patient sample

- Patients with osteoporosis who received ongoing care in an EMR practice site were included if they were observable for at least 1 year prior to the date on which they first met criteria for being both postmenopausal and having osteoporosis
 - *Postmenopausal status* – age ≥50 years, a mention of postmenopausal status, or pharmacotherapy related to menopause
 - *Osteoporosis* – a diagnosis of osteoporosis or osteoporotic fracture, a bone mineral density (BMD) t-score ≤-2.5, or pharmacotherapy related to osteoporosis

Clinical risk factors

- Age
- Bone mineral density (BMD)
- Body mass index (BMI)
- Personal history of fracture
- Maternal history of osteoporosis or fracture

Statistical analysis

- Cox Proportional Hazards Models were used to estimate the risk of fracture associated with each clinical risk factor alone, adjusted for the other risk factors, and adjusted for disease and treatment variables
- Descriptive and inferential statistics were performed using SAS® version 9.1
- An *a priori* alpha level of 0.05 was used to determine statistical significance

Results

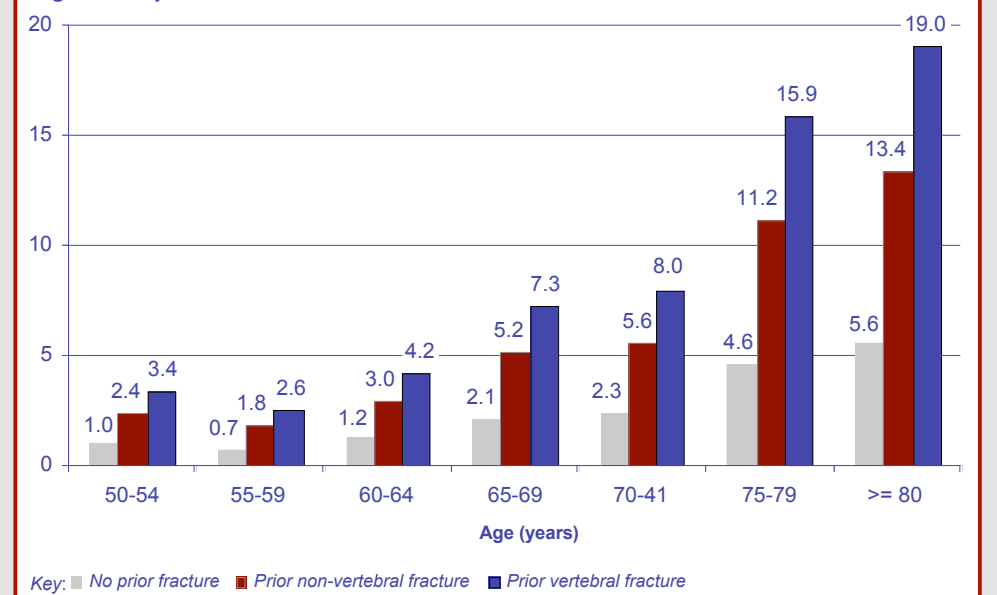
- Of the 190,847 women in the EMR database a total of 50,783 patients were post-menopausal and had osteoporosis or were receiving osteoporosis-related treatments
- Baseline characteristics and hazards for vertebral fracture are shown in Table 1
- Increasing age and prior fragility fractures since age 50 were associated with a substantial increase in fracture risk
- Combined hazards for VF were substantially higher for older patients with prior fractures, as shown in Figure 1

Table 1. Patient characteristics, risk factors, and hazards for vertebral fracture

Risk Factor	N	(%)	Univariate HR	Unadjusted HR	Adjusted HR*
Age category 50,783					
50-54	5,283	(10.4)	Reference		
55-59	7,551	(14.9)	0.77	0.76	0.75
60-64	7,439	(14.7)	1.38	1.38	1.25
65-69	7,771	(15.3)	2.55†	2.52†	2.17†
70-74	9,823	(19.3)	3.08†	2.97†	2.40†
75-79	11,845	(23.3)	6.85†	6.41†	4.79†
≥80	1,071	(2.1)	9.06†	7.90†	5.82†
BMI 42,446					
Extremely obese	1,143	(2.7)	Reference		
Obese	8,204	(19.3)	1.25		
Overweight	14,337	(33.8)	1.14		
Normal	17,576	(41.4)	1.38		
Underweight	1,186	(2.8)	2.29†		
BMD T-score 3,431					
High normal	101	(2.9)	2.58		
Normal	641	(18.7)	0.44		
Osteopenia	1,799	(52.4)	Reference		
Osteoporosis	890	(25.9)	1.22		
History of Fracture 50,783					
Any fracture	1,769	(3.5)	3.59†		
Hip fracture	377	(0.7)	3.01†		
Non-vertebral fracture	1,027	(2.0)		2.42†	1.61†
Other fracture	486	(1.0)	3.39†		
Vertebral fracture	742	(1.5)	4.69†	3.43†	3.03†
Wrist fracture	299	(0.6)	2.13†		
Race 15,679					
Caucasian	12,974	(82.8)	Reference		
Black	958	(6.1)	0.59		
Hispanic	1041	(6.6)	0.48†		
Asian	559	(3.6)	0.26		
Other	138	(0.9)	1.10		

Key: BMI – body mass index defined as ≥40 kg/m²=extremely obese, 30-39.9=obese, 25-29.9=overweight, 18.5-24.9=normal, <18.5=underweight; BMD – bone mineral density (T-scores defined as >+1=high normal, ≥-1 and ≤+1=normal, ≥-2.5 and <-1=osteopenia, <-2.5=osteoporosis; Other fracture- fracture excluding vertebral, wrist and hip fractures
* Adjusted for disease and treatment covariates
† P-value <0.05

Figure 1. Adjusted hazards for vertebral fracture for combined risk factors



Conclusions

- A prior VF was associated with a 3-fold increased risk of incident VF in the EMR population
- Risk increases were markedly higher for older women with prior fractures
- BMI was not a significant predictor of VF in this analysis and may not be a valid predictor in a largely overweight population

Limitation

- BMD was reported in only a small proportion of the EMR population (6.8%) and that may have resulted in an inability to determine the association between low BMD and VF risk due to reporting bias

References

1. Siris ES, Brennan SK, Miller PD, Barrett-Connor E, Chen YT, Sherwood LM, Abbott TA. Predictive value of low BMD for 1-year fracture outcomes is similar for postmenopausal women ages 50-64 and 65 and Older: results from the National Osteoporosis Risk Assessment (NORA). JBMR. 2004;19(8):1215-20.

Acknowledgement

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