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Height Loss, Vertebral Fractures, and the Misclassification of Osteoporosis

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Abstract

Background—The presence of a vertebral fracture identifies a patient who has clinical osteoporosis. However, approximately 2/3 to 3/4 of VFs are asymptomatic. Vertebral Fracture Assessment is a method derived from dual-xray absorptiometry (DXA) to assess vertebral fractures. The objectives of this study were 1) to determine the association between the degree of height loss in older men and women and risk of a vertebral fracture, and 2) to determine if knowledge of vertebral fractures will alter the classification of osteoporosis based on bone mineral density alone.

Methods—231 men and women over the age of 65 underwent DXA scan of their spine and hip (including bone mineral density and Vertebral Fracture Assessment), measurement of their height, and a questionnaire.

Results—We found that height loss was significantly associated with a vertebral fracture ($p=0.0160$). The magnitude of the association translates to a 19% increase in odds for 1/2 inch and 177% for 3 inches. Although 45% had osteoporosis by either bone mineral density or fracture criteria, 30% would have been misclassified if bone mineral density criteria were used alone.

Conclusions—Height loss is an indicator for the presence of vertebral fractures. Bone mineral density criteria alone may misclassify older patients who have osteoporosis.

Keywords

vertebral fractures; vertebral fracture assessment; osteoporosis; bone mineral density

1. Introduction

In addition to low bone mass, a previous fracture significantly increases the risk of developing a future fracture. A vertebral fracture increases the risk of a new fracture up to 4-fold (1–4). In addition to needing therapy, patients with vertebral fractures may suffer from increased back pain, increased days of bed rest, decreased time at work, depression, and a

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higher rate of hospitalization and mortality (5;6). Thus, the presence of a vertebral fracture has significant clinical impact.

Approximately two-thirds to three-quarters of vertebral fractures are asymptomatic (7). Diagnosis of an asymptomatic vertebral fracture is not common in clinical practice, because it requires a lateral x-ray, often performed at a different facility (hospital or radiology unit) and increases the patient's expense and radiation exposure. By contrast, Vertebral Fracture Assessment (VFA) is a dual-energy X-ray absorptiometry (DXA)-based technology that can be performed at the same point of service during bone density assessment and uses a much lower radiation dose than a standard lateral X-ray. Greenspan et al. has previously found that vertebral fractures assessed by VFA were present in 18.3% of asymptomatic, postmenopausal women who were screened for osteoporosis by DXA (8). When using BMD to classify osteoporosis using the World Health Organization classification, sensitivity ranged from 40 to 74%. When VFA was included to classify patients with osteoporosis, as much as 60% of osteoporotic individuals would have been missed by BMD alone. Therefore, VFA may be a useful adjunct in the clinical identification of osteoporosis and may prevent mismanagement of osteoporotic patients.

The International Society of Clinical Densitometry has suggested indications for VFA including women who have had a height loss from peak height of ≥ 1.6 inches, men who have had a height loss of ≥ 2.4 inches, or patients with prospective height loss of >0.8 inches in women or >1.2 inches in men (9). However additional data are needed to support these recommendations. The objective of this study was to determine the association between degree of height loss in both older men and women and risk of a vertebral fracture, and to determine if VFA will increase the prevalence of osteoporosis diagnosis in men and women who are being screened for osteoporosis by BMD alone.

2. Material and Methods

2.1 Study subjects

Two hundred and thirty-one men and women over the age of 65 were recruited from the Claude D. Pepper Registry, Benedum Geriatric Clinic at University of Pittsburgh Medical Center, Braddock Hospital, and through advertising. The Claude D. Pepper Registry is a database of more than 2,000 Pittsburgh participants over the age of 60 who are willing to participate in research. Reasons for exclusion were morphological abnormalities, metabolic bone disease other than osteoporosis, and consumption of medication that affect bone mineral metabolism positively or negatively other than calcium and vitamin D. The study was approved by the institutional review board at the University of Pittsburgh Medical Center, PA, and all participants signed written informed consent.

2.2 Outcome variables

Bone mineral densitometry of the PA spine and hip were assessed by dual-energy X-ray absorptiometry (DXA) using a Hologic Discovery A bone densitometer located in the Benedum Geriatric Clinic and the Clinical Translational Research Center at University of Pittsburgh Medical Center. Measurements were obtained and analyzed using standard manufacturer protocols. World Health Organization (WHO) criteria were used to classify bone health and osteoporosis (10). T-score of $-1.0SD$ and above is considered normal, T-score between $-1.0SD$ and $-2.5SD$ is considered low bone mass (osteopenia), and T-score of $-2.5SD$ and below is considered osteoporotic (11). Bone mineral density measurements were taken for the spine, total hip, and the femoral neck as suggested by recommendations of the International Society for Clinical Densitometry (12). The site with the lowest T-score was included in the classification of osteoporosis.

VFA was performed through lateral spine imaging of T4-L4 on Hologic Discovery A using manufacturer standard protocols. The vertebral bodies from the scan were visually inspected by a technician and fractures were classified using the method of Genent (semiquantitative visual assessment) with the assessment of computer-calculated reduction in vertebral height (13). Two technicians trained in VFA examined VFA results independently and were blinded to the BMD results. If differences were noted, the VFA was reanalyzed by both technicians together.

2.3 Clinical Characteristics

A questionnaire was administered that contained medical, surgical, gynecological, fracture, and family history in addition to medications, alcohol, tobacco, and exercise. Participants were also asked to report their tallest height ever from memory. Nontraumatic fragility fractures were defined as fractures that occurred from a fall from standing height or lower. Known traumatic nonvertebral fractures were excluded. Current height was measured 3 times with a Harpenden stadiometer and an average was calculated. Participants' height loss was calculated as tallest height ever minus current height.

2.4 Statistical analysis

The presence of vertebral fractures was operationally defined as a dichotomous variable indicating one or more and three or more fractures. We compared characteristics of subjects with and without VF using independent samples *t*- and chi-square tests, as appropriate, for continuous and categorical measures. We used logistic regression models with the presence of vertebral fractures as the dependent variable, height loss as the primary predictor variable of interest, and exercise, smoking, and calcium/vitamin D intakes covariates. The logistic regression coefficient for height loss was scaled appropriately and then exponentiated to obtain odds ratios for magnitudes of risk increases corresponding to a height loss between 1/2 inch and 3 inches. We used a two-way contingency table cross tabulation of subjects meeting criteria of osteoporosis using BMD alone by VF alone. All analyses were performed both with and without stratification by gender. We used SAS[®] version 9.2 (SAS Institute, Inc., Cary, North Carolina) for all statistical analyses.

3. Results

We recruited 231 participants, including 124 men and 107 women. The average age was 75 ± 6 years and their average height loss from peak was 1.86 ± 1.22 inches (mean $\pm$ SD). Ninety-one participants had one or more vertebral fractures and 20 had three or more vertebral fractures. Twenty-one percent had a previous history of an adult fragility fracture (including 3 with a hip fracture), 77% participated in exercise, and 58% took calcium and vitamin D supplements. There were no significant differences between men and women in terms of their vertebral fracture rate (Table 1). However, those who exercised were less likely to have one or more vertebral fractures than those who did not (35% with exercise vs 54% with no exercise, $p=0.014$). Furthermore, those with 3 or more vertebral fractures were less likely to take calcium and vitamin D (5%) than those who did not (13%, $p=0.029$) (Table 2).

Participants with one or more vertebral fractures had greater height loss (mean 2.18 ± 1.30 inches) than subjects without vertebral fractures (1.64 ± 1.11 inches). Forty-three percent of women had one or more VF and 36% of men had one or more vertebral fractures. In women, those with no VF had an average height loss of 1.54 inches, whereas those with one or more vertebral fractures had lost an average of 2.07 inches ($p=0.0184$). In men, those with no vertebral fracture had an average height loss of 1.72 inches, whereas those with one or more vertebral fractures had lost an average of 2.30 inches ($p=0.0146$). For each additional 0.5

inch of height loss, the odds ratios for having one or more vertebral fractures increased significantly when adjusted for smoking, exercise, calcium, and vitamin D intake (OR = 1.19, 1.40, 1.66, 1.97, 2.34, 2.77, $p < 0.05$) (Table 3).

According to WHO classification, 60 out of 107 women (56%) from our study had low bone mass and 23 out of 107 (22%) had osteoporosis, compared to 64 out of 124 (52%) and 10 out of 124 (8%) for men, respectively (Table 4). The prevalence of osteoporosis varied when defined by BMD site only vs. BMD site and vertebral fractures combined. For example, 29 out of 231 participants (12.6%) were categorized as osteoporotic when using femoral neck BMD as the sole criteria, but 101 out of 231 participants (43.7%) were categorized as osteoporotic when using femoral neck BMD and vertebral fracture as criteria (Table 4).

In all our participants, 91 out of 231 (39%) had one or more vertebral fractures, and 20 out of 231 (9%) had three or more vertebral fractures (Table 1). Twenty-eight out of 74 subjects (38%) who were categorized as normal by BMD and 42 out of 124 subjects (34%) who were categorized as having low bone mass had one or more vertebral fractures (Figure 1). In patients with one or more vertebral fractures, the distribution of a normal or low bone mass classification was similar in men and women. One hundred and three out of 231 patients (45%) had osteoporosis by BMD classification or presence of a vertebral fracture (Table 5). If BMD classification was used alone, 70 out of 231 total participants (30%) would have been misclassified (Table 5). If we exclude 3 patients who had a hip fracture and who should have been classified with clinical osteoporosis by NOF guidelines, in the remaining 228 participants, 69/228 or 30% would have been misclassified.

4. Discussion

We found that height loss was significantly associated with a vertebral fracture. The magnitude of the association translates to a 19% increase in odds of having a vertebral fracture for 1/2 inch of height loss and 177% for 3 inches. Those with a vertebral fracture, on average, had a 0.54 inch greater height loss than those without a vertebral fracture. Although 45% had osteoporosis by either BMD or fracture criteria, 30% would have been misclassified if BMD criteria was used alone.

Similar to studies by Siminoski et al, our study showed that the relationship between height loss and prevalent vertebral fractures was significant (14). Our study also agreed with the cross-sectional studies by Tobias et al, and Gunnes et al which determined that prevalent vertebral fracture rates increased with greater height loss (15;16). In the study by Tobias et al where they included 509 women, the difference in height loss between the two groups was 0.31 inches. Our participants with one or more vertebral fractures lost an average height of 0.54 inches more than our participants with no vertebral fractures.

Prospective studies have also demonstrated a correlation between height loss and incident fractures. Moayyeri et al (17) recruited 25,623 men and women 40–79 years old, measured their height and followed their fracture status over several years. The study showed that height loss is an independent risk factor for osteoporotic fractures. Kaptoge et al (18) showed that the risk of incident vertebral fracture significantly increased with increased height loss. Some studies have suggested a height loss cutoff to indicate increased risk of vertebral fractures. Due to the small number of participants, we were unable to find a statistically significant threshold value. However, our data did suggest a sharp increase in the number of vertebral fractures once participants have lost more than 3 inches. This finding is similar to that of Vallarta-Ast et al (19) who found an increase in fracture prevalence in men when the historical height loss > 2.5 inches and also to that of Siminoski, who suggested the cutoff to be 6cm (2.4 inches). Siminoski conceded that height loss was

not a good screening test for vertebral fracture because it had low sensitivity values and high specificity. Combined with other risk factors, such as age and previous history of fractures, the sensitivity of predicting vertebral fractures may be higher (15;20).

Our study differed from others that looked at vertebral fractures and height loss. Unlike the study by Siminoski et al, our study excluded participants with metabolic bone diseases and those taking bone-altering medications. Unlike the study by Tobias et al and Gunnes et al, our study included both men and women over the age of 65 with no upper age limit. Compared to previous studies, the prevalent vertebral fracture rate in our study was higher: thirty-six percent of men and 43% of women had one or more vertebral fractures. When using BMD WHO classification and presence of vertebral fractures as criteria for diagnosing osteoporosis, as many as 51% of women and 39% of men had osteoporosis. In Tibias et al, UK women 65–76 years old were recruited; 7.3% of the 509 subjects had one or more vertebral fractures. They identified vertebral fractures with standard X-ray, while we used VFA. However, previous studies have documented that vertebral fractures are often missed on X-rays (21). Our VFA criteria used a quantitative assessment and identified a vertebral fracture with a loss of height of 20% or more. This quantitative assessment differs from the qualitative technique used by many radiologists. The prevalence of osteoporosis in our population was also higher than those reported by Cheng et al who reviewed Medicare claims data of 911,327 beneficiaries over the age of 65. Cheng's paper estimated 41.8% of Caucasian females between 75–79 years have osteoporosis, and 8.4% Caucasian males between 75–79 years have osteoporosis. In addition to the quantitative technique, our higher rates of osteoporosis may be explained by the fact that many of our patients were recruited from Benedum Geriatric Clinic. Patients who visit the clinic tend to be more frail, more likely to have fractures, and be osteoporotic. Furthermore, we obtained VFA to assess for vertebral fractures while Medicare claim data could miss asymptomatic fractures. Our high male osteoporotic rate may also be due to the fact that only a minority of vertebral fractures in men comes to clinical attention, contributing to lower rates seen through insurance claims.

Our study demonstrated that men and women with vertebral fractures were often misclassified as having normal or low bone mass by BMD alone. In a study by Freitas et al, 5995 men were recruited and out of those with incident vertebral fractures, 41% had normal BMDs and 46% were categorized as having low bone mass (22). Similarly, the Rotterdam study by Schuit et al showed that many women and men with non-vertebral fractures were categorized as normal or having low bone mass by BMD alone (23). They concluded that BMD needs to be used with other predictors of fractures -- such as height loss -- to increase its sensitivity. We suggest that in addition to clinical risk factors such as height loss, the VFA is a useful adjunct to BMD and may prevent misdiagnosis of osteoporosis in men and women.

Because this is a cross-sectional study, we can not determine cause and effect. Although we observed that those who exercised were less likely to have vertebral fractures than those who did not exercise, patients with fractures may be less likely or able to exercise after they fracture. We observed that patients with 3 or more fractures were less likely to take calcium and vitamin D. However due to other comorbid conditions in these patients, they may be less likely to comply with calcium and vitamin D. Furthermore we could not determine if these vertebral fractures were caused by a previous high trauma accident. We did however query participants for known traumatic fractures and only included nontraumatic fragility fractures by their history. A prospective study is needed to corroborate these cross-sectional findings.

This study has many strengths. It is one of the few studies that compare BMD, height loss, and vertebral fractures in both men and women from the same population. Our population

included men and women in many stages of health. We recruited healthy, active volunteers as well as frail visitors to the Benedum Geriatric Clinic. Our study also has several limitations. The sample size is small. There may also be selection bias because many of our patients came from Benedum Geriatric Clinic and may be more frail than the general population. Our results may not be applicable to people <65 years old and not applicable to minorities since most of our participants were Caucasian. Moreover our study may be subject to recall bias regarding a patient's previous height. Finally, we did not verify vertebral fractures with a standard x-ray. However, the VFA technique has been validated in the past for moderate and severe vertebral fractures (24;25).

In summary, height loss is an indicator for the presence of vertebral fractures; and the Vertebral Fracture Assessment increases the prevalence of osteoporosis diagnosis in men and women who are being screened for osteoporosis by Bone Mineral Density alone. Those misclassified by BMD alone – 30% of all participants--were correctly classified after having a VFA performed. Further studies are needed to assess longitudinal height loss and incident vertebral fractures assessed by VFA in other clinically relevant cohorts.

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Figure 1.

The percentage of participants classified with normal, low bone mass or osteoporosis by Bone Mineral Density who had zero (0 VF), one (1 VF) or two or more vertebral fractures (2+ VF) by Vertebral Fracture Assessment.

Table 1

Clinical Characteristics

	Total	Men	Women
# Participants (%)	231	124 (54%)	107 (46%)
Age (years)	75 ± 6	75 ± 6	75 ± 7
Average Height loss (inches)	1.86 ± 1.22	1.93 ± 1.26	1.77 ± 1.17
Average % height loss	2.75% ± 1.79%	2.75% ± 1.79%	2.75% ± 1.80%
Average BMI (kg/m ²)	29 ± 5	28 ± 5	29 ± 6
# with 1+ vertebral fracture (%)	91 (39%)	45 (36%)	46 (43%)
# with 3+ vertebral fracture (%)	20 (9%)	9 (7%)	11 (10%)
History of fragility fractures	49 (21%)	15 (12%)	34 (32%)
Smoking (%)	116 (50%)	82 (66%)	34 (32%)
Exercise (%)	177 (77%)	111 (90%)	66 (62%)
Calcium intake	134 (58%)	64 (52%)	70 (65%)
Vitamin D intake	134 (58%)	64 (52%)	70 (65%)

Results: mean ± SD or N (%)

Table 2

Rates of having VFs based on exercise, smoking, and calcium/vitamin D intake

		Rate of having 1 or more VFs	P value	Rate of having 3 or more VFs	P value
All	Exercise	35%	0.014	7%	>0.05
	No exercise	54%		13%	
	Smoking	38%	>0.05	7%	>0.05
	No smoking	41%		10%	
	Ca/VitD	34%	>0.05	5%	0.029
	No Ca/VitD	46%		13%	
Women	Exercise	30%	0.0008	6%	>0.05
	No exercise	63%		17%	
	Smoking	38%	>0.05	6%	>0.05
	No smoking	45%		12%	
	Ca/VitD	40%	>0.05	9%	>0.05
	No Ca/VitD	49%		14%	
Men	Exercise	38%	>0.05	8%	>0.05
	No exercise	23%		0%	
	Smoking	38%	>0.05	7%	>0.05
	No smoking	33%		7%	
	Ca/VitD	28%	0.0508	2%	0.0116
	No Ca/VitD	45%		13%	

Table 3

Height loss and odds of having a vertebral fracture*

Unit of Height Loss (inches)	Odds Ratio	95% Confidence Limits
0.5	1.19	1.06 – 1.34
1	1.40	1.12 – 1.79
1.5	1.66	0.71 – 2.15
2	1.97	0.64 – 2.77
2.5	2.34	0.57 – 3.58
3.0	2.77	0.51 – 4.61

P < 0.05

* adjusted for smoking, exercise, and Vitamin D intake

Table 4

Prevalence of Osteoporosis by WHO BMD Classification

	Spine Only	Total Hip Only	Femoral Neck Only	Any Site
All				
BMD with vertebral fracture (true classification)				
Osteoporosis	42.4%	41.1%	43.7%	45.0%
Low Bone Mass	16.5%	17.7%	33.8%	35.1%
Normal	41.1%	41.1%	22.5%	19.9%
BMD alone				
Osteoporosis	6.5%	3.5%	12.6%	14.7%
Low Bone Mass	26.4%	34.2%	52.4%	53.2%
Normal	67.1%	62.3%	35.1%	32.0%
Men				
BMD with vertebral fracture (true classification)				
Osteoporosis	38.7%	36.3%	37.1%	38.7%
Low Bone Mass	12.9%	13.7%	35.5%	35.5%
Normal	48.4%	50.0%	27.4%	25.8%
BMD alone				
Osteoporosis	4.0%	1.6%	5.6%	8.1%
Low Bone Mass	20.2%	25.8%	52.4%	51.6%
Normal	75.8%	72.6%	41.9%	40.3%
Women				
BMD with vertebral fracture (true classification)				
Osteoporosis	46.7%	46.7%	51.4%	51.4%
Low Bone Mass	20.6%	22.4%	31.8%	35.5%
Normal	32.7%	30.8%	16.8%	13.1%
BMD alone				
Osteoporosis	9.3%	5.6%	20.6%	21.5%
Low Bone Mass	33.6%	43.9%	52.3%	56.1%
Normal	57.0%	50.5%	27.1%	22.4%

Table 5

Misclassification of Osteoporosis

	No VF	Yes VF	Total
BMD: Normal or Low Bone Mass	128	70	198
BMD: Osteoporosis	12	21	33
Total	140	91	231