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Changes in Bone Mineral Density (BMD) May Predict the Risk of Fracture Differently in Older Adults According to Fall History

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Abstract

Objectives—To determine whether the association between BMD change over 4 years and risk of hip and non-vertebral fracture differs according to an individual's history of falls.

Design—cohort study.

Setting—population based from Framingham, MA.

Participants—310 men and 492 women with two measures of BMD at the femoral neck (mean age 78.8 years).

Measurements—Cox proportional hazards models were used to estimate hazard ratios (HR) for the association between percent BMD change (per sex-specific standard deviation) and risk of incident hip and non-vertebral fracture. Models were stratified based on history of falls (1 fall in the past year) and recurrent falls (2 falls) ascertained at the time of the second BMD test. Interactions were tested by including the term 'fall history * BMD change' in the models.

Results—Mean BMD change was -0.6% /year. Falls were reported by 27.8% of participants, and 10.8% reported recurrent falls. 76 incident hip and 175 incident non-vertebral fractures occurred over median followup 9.0 years. There was no difference in the association between BMD change and hip fracture according to history of falls (p for interaction= 0.57). In participants without a history of falls, the HR associated with BMD change and non-vertebral fracture was 1.31 (95% CI 1.10, 1.56) compared with HR 0.95 in those with a fall (95% CI 0.70, 1.28; interaction $p=0.07$). Results for recurrent fallers were similar.

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Author Contributions: Dr. Berry and Dr. Kiel conceived of the study idea. Dr. Kiel and Dr. Cupples were responsible for providing the data. Dr. Berry had access to all of the data, and she is responsible for the accuracy of the data. All authors participated in the interpretation of the analyses. Dr. Berry drafted the manuscript. All authors participated in substantial revision of the manuscript.

Conclusion—Our results suggest the effect of BMD loss on risk of non-vertebral fracture may be greater in persons without a history of falls. It is possible that BMD change contributes less to fracture risk when a strong risk factor for fracture, such as falls, is present.

Keywords

bone mineral density (BMD) change; hip fracture; non-vertebral fracture; falls; recurrent falls

Introduction

Low bone mineral density (BMD), increases the risk of fracture at the hip, spine, shoulder, wrist, and other skeletal sites.^{1–3} Osteoporosis medications are effective in reducing the risk of fracture among persons with low BMD and other clinical risk factors for fracture, even among persons aged 75 years and older.^{4–7} Thus, it is recommended that women ≥65 years of age^{8, 9} and men ≥70 years of age⁹ are screened for osteoporosis with BMD as measured by central (hip or spine) dual-energy x-ray absorptiometry (DXA).

Despite the value of BMD in the management of osteoporosis, recent studies have challenged the utility of repeating a BMD screening test over a short time interval. For example, our group previously reported that on average, BMD change over 4 years provided little additional value beyond baseline BMD when predicting risk of hip and major osteoporotic fracture.¹⁰

It is important to identify clinical characteristics that are strong determinants of fracture risk, such as falls, that could inform the decision of whether to repeat a BMD screening test. Our primary objective was to determine whether BMD change over 4 years affected the risk of hip and non-vertebral fracture differently according to an individual's history of falls in women and men from the Framingham Osteoporosis Study. We hypothesized that BMD change would be more strongly associated with risk of fracture among individuals with a history of falls or recurrent falls.

Methods

Participants

The Framingham Original Cohort began in 1948 with enrollment of 5,209 men and women recruited from a two-thirds sample of the town Framingham, MA.¹¹ Since 1948 these participants have been examined every two years. Between 1987–1999, all surviving participants were invited for three rounds of BMD testing, approximately 4 years apart. Participants of the current study included 802 members with two measures of femoral neck BMD free of hip fracture at the time of the second BMD test. Study details have previously been published.¹⁰ The mean time between BMD tests was 3.7 years (range 2.4 – 6.0 years).

Bone mineral density (BMD)

BMD of the femoral neck (g/cm^2) was measured using a Lunar dual photon absorptiometer (DP3) between 1987–1991 and a Lunar dual energy x-ray absorptiometer (DPX-L) between 1992–1999, with adjustments made using the cross-calibration of the two instruments.¹² The

coefficients of variation for the individual scanners ranged from 1.7% to 2.6% at the femoral neck. We calculated annualized percent BMD change for each participant as follows: $[(BMD_2 - BMD_1)/BMD_1] * 100 / \text{time (in years)}$ between assessments.

Falls

Falls in the past year were ascertained by self report at the clinic examination just preceding the second BMD test (Figure 1). Participants were categorized as having had a history of falls (any fall in the past year) versus no history of falls. Participants were also classified as having recurrent falls (≥ 2 falls in the past year) or no recurrent falls (none or 1 fall in the past year). One participant reported falling without recording the number of falls, and this participant was excluded from the recurrent falls analyses.

Hip and other non-vertebral fractures

Hip fractures were defined as non-traumatic incident fractures of the proximal femur that occurred after the second BMD test, and fractures were confirmed with medical records.¹³ Non-vertebral fractures at sites other than hip were not confirmed by medical record review. These included all fractures except the spine, fingers, toes, skull, or face.

Clinical characteristics

Information on clinical characteristics was obtained from the Framingham study examination closest to and preceding the second BMD test. Weight, measured to the nearest pound in light clothing, and height without shoes, measured to the nearest quarter-inch, were used to calculate body mass index, or BMI (kg/m^2). Prior non-hip fracture included any self-reported fracture except the hip, fingers, toes, skull, or face occurring as an adult but before the second BMD test.

Statistical analysis

We described characteristics of study participants according to their history of falls. Participants were followed from the second BMD measure until death, incident hip or non-vertebral fracture, or through 2009 for a maximum of 12-years followup. We used Cox proportional hazards models to calculate hazard ratios (HR) and 95% confidence intervals (CI) to estimate the association between percent BMD change (per sex-specific standard deviation) and risk of incident hip and non-vertebral fracture. Models were adjusted for baseline BMD as well as age, sex, BMI, and prior non-hip fracture as measured at the time of the second BMD exam. Models were stratified based on history of falls and recurrent falls. Interactions were tested by including the term 'fall history * BMD change' in the models. We used SAS version 9.3 for all analyses (SAS Institute, Inc., Cary, NC).

Results

Participants in the current study included 310 men and 492 women. Mean age at the time of the second BMD test was 78.8 ± 4.5 years. Mean BMD change was -0.6% /year, and ranged from 5.6% /year (gain) to -9.0% /year (loss). Nearly 28% of participants reported a fall in the past year, and 10.9% of participants reported recurrent falls.

Participants with a history of falls were older, more likely to be male, and more likely to report a prior history of a fracture as compared with participants without a history of a fall (Table 1). Baseline BMD and annualized % BMD change were similar among individuals with and without a history of falls. However, participants with a history of recurrent falls experienced more bone loss as compared with participants with no falls (−0.9% versus 0.6%).

During a median followup of 9.0 years, 76 participants experienced an incident hip fracture and 175 participants experienced an incident non-vertebral fracture. The most frequent type of incident non-vertebral fracture was hip, followed by wrist (n=20), humerus (n=14), ribs (n=13), leg (n=13), pelvis (n=9), ankle (n=9), clavicle (n=8), foot (n=6), hand (n=4), knee (n=2), and sternum (n=1).

Annualized percent BMD change was associated with an increased risk of hip fracture after adjusting for baseline BMD and other clinical characteristics (HR for every standard deviation (SD) decrease in BMD=1.43; 95% CI, 1.16, 1.78). Results were similar when stratified by history of falls (Table 2). There was a suggestion that the association between BMD percent change and risk of hip fracture was stronger in participants without recurrent falls (HR for every SD decrease in BMD=1.50; 95% CI 1.20, 1.88) as compared to participants with recurrent falls (HR for every SD decrease in BMD=1.09; 95% CI 0.55, 2.16). The interaction term, however, for BMD change and recurrent falls history was not statistically significant (p=0.22).

For non-vertebral fractures, every standard deviation decrease in annual percent BMD change was associated with an increased risk of fracture (HR=1.20; 95% CI 1.03, 1.39). The association between BMD percent change and risk of non-vertebral fracture was stronger in participants without a history of falls (HR=1.31 for every SD percent decrease; 95% CI 1.10, 1.56) as compared to those with a history of falls (HR=0.95 for each SD percent decrease; 0.70, 1.28). The interaction term for BMD change and history of falls approached statistical significance (p=0.07). A similar trend was observed when models were stratified by a history of recurrent falls.

Discussion

The utility of repeating a BMD screening test over a short time interval is contentious. For many older adults, a baseline BMD measure will suggest that pharmacologic treatment is indicated,¹⁴ and repeat BMD screening may not change clinical management. Even among screened adults who do not initially meet pharmacologic treatment criteria, rescreening at a later date utilizing the Fracture Risk Assessment Tool (FRAX) with historic BMD and updated clinical characteristics may alter treatment recommendations such that repeating a BMD test is unnecessary.

For the remaining individuals in whom a repeat BMD test could change management, there is no guidance on what clinical characteristics could be used to guide testing. We examined whether fall history differentially affected the association between BMD change and risk of fracture. Interestingly, our results suggest that the impact of bone loss on risk of non-

vertebral fracture may be greater in persons without a history of fall. Further, BMD loss may increase the risk of hip and non-vertebral fracture in persons without recurrent falls, but not in persons with recurrent falls. This suggests that untreated individuals without a history of falls may benefit more from repeating a BMD screening test as compared to individuals with a history of falls.

It is possible that our unexpected findings could have arisen if BMD change contributes less to fracture risk when a strong risk factor for fracture, such as falls, is present. In a retrospective cohort study in Belgium, Geusens et al. found that falls were a more important risk factor for non-traumatic fractures than radial BMD.¹⁵ In this study, post-menopausal women with a mean age of 61 years and a T-score between -1 and -2.5 (osteopenia) with no history of falls were at 2.8 times (95% CI 0.9, 8.9) increased risk of fracture as compared to women with normal BMD and no history of falls. In comparison, women with osteopenia and a history of falls had a 21.0 fold (95% CI 7.1, 62.3) increased risk of fracture. In a second large, multicenter European study by Kaptoge et al., the authors concluded that femoral neck BMD explains less of the variation in risk of upper extremity fracture in women as compared with a history of falls or clinical characteristics strongly associated with the opportunity to fall, such as time spent walking.¹⁶ However, femoral neck BMD explained more of the variation in risk of all fracture types than did falls history in women and men. Thus, while an intriguing hypothesis, we suggest that our results be replicated before recommending that fall status be used to determine whether repeat BMD testing is necessary.

The difference in the association between BMD change and risk of non-vertebral fracture in fallers and non-fallers merely approached statistical significance in our study, and it is possible that this difference occurred by chance. The finding that fall history did not modify the association between BMD change and risk for hip fracture may have been due to the small number of hip fractures observed in our study. It is also possible that we were unable to detect any association between BMD change and fracture among fallers because fallers experienced more bone loss. Stratifying according to falls status may have already accounted for BMD change in this high risk group, and thus, a distinct association between BMD change and fracture may not have been observed.

The strengths of this study include a large, population-based sample of older men and women with two BMD measures approximately 4 years apart and a history of falls obtained at approximately the same time as the second BMD measure.

There are also limitations of this study. First, our results regarding fracture risk in non fallers was only of borderline statistical significance. Second, it is possible that some misclassification of BMD change and falls history exists. BMD was measured on two different instruments for most participants. Adjustments were made using previously published calibrations,¹² but inter- and intra- machine precision error could result in misclassification of BMD change. Falls history was self reported in the past year, and it may underestimate the true prevalence of falls. We would expect these types of misclassification would make it less likely that we would find a difference in the effect of BMD change according to falls history as all participants were scanned on the same two devices and falls

history was ascertained independent of the BMD measures. Thus, the differential effect of BMD change that we observed may be conservative. Third, we did not have information on the prevalence of osteoporosis drug use. We expect use was low during the time of our study, but importantly, our results may not generalize to a treated population. Fourth, our results reflect the value of self reported falls in the past year, and we cannot address the importance of more remote falls when considering a BMD screening test. Finally, our study was comprised of whites, and the significance of repeating a BMD measure according to falls status may differ in other ethnic populations.

In conclusion, BMD loss may be more important in the prediction of hip and non-vertebral fracture in individuals without a history of falls as compared with individuals with a history of recurrent falls. Confirmation of these findings is needed before recommending that fall status be used to determine whether a repeat BMD screening test should be performed.

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Figure 1.

Schematic diagram of the study design. All participants had a baseline BMD test (1987–1997) and a second BMD test (1992–1999). Falls history was ascertained near the time of the second BMD test. Participants were followed from the time of the second BMD test until the first occurrence of hip or non-vertebral fracture, death, or until the end of study (12/31/2009 or 12-years of followup).

Table 1

Characteristics of 802 participants of the Framingham Osteoporosis Study with two measures of BMD, according to history of falls^a

	No history of fall	<u>History of falls in the year prior to the second BMD test</u>	
	n=579	Any falls (1) n=223	Recurrent falls ^b (2) n=87
Age, yrs	78.4 ± 4.2	79.6 ± 5.0	80.0 ± 5.4
Male (%)	219 (37.8)	91 (40.8)	29 (33.3)
BMI, kg/m ²	26.7 ± 4.5	27.2 ± 5.0	27.2 ± 5.2
Prior fracture (%)	166 (28.7)	90 (40.4)	37 (42.5)
Baseline BMD, g/cm ²	0.79 ± 0.14	0.79 ± 0.15	0.79 ± 0.17
Annualized % BMD change	-0.6 ± 1.8	-0.6 ± 1.8	-0.9 ± 1.9
Experienced hip fracture during followup (%)	55 (9.5)	21 (9.4)	9 (10.3)
Experienced non-vertebral fracture during followup (%)	117 (20.2)	58 (26.0)	19 (21.8)

^aFalls ascertained at the time of the second BMD test

^bRecurrent falls is not a mutually exclusive classification. Participants with recurrent falls are included in the “any falls” classification

Table 2

Hazard ratios (HR)^a and 95% confidence intervals (CI) to describe the association between BMD change and risk of hip or non-vertebral fracture, according to falls history

	Hip Fracture			Non vertebral Fracture		
	# fractures/#participants	Multivariable adjusted HR (95% CI)	p-value Fall*BMD interaction	# fractures/#participants	Multivariable adjusted HR (95% CI)	p-value Fall*BMD interaction
Any falls	21/223	1.50 (1.17, 1.92)	0.57	58/223	0.95 (0.70, 1.28)	0.07
No falls	55/579	1.40 (0.88, 2.23)		117/579	1.31 (1.10, 1.56)	
Recurrent falls ^c	9/87	1.09 (0.55, 2.16)	0.22	19/87	0.71 (0.41, 1.22)	0.15
No recurrent falls	67/714	1.50 (1.20, 1.88)		156/714	1.25 (1.07, 1.46)	

^a Adjusted for baseline BMD plus age (yrs), sex, BMI (kg/m²), and prior non-hip fracture as measured at the time of the second BMD test

^b Per standard deviation decrease in percent BMD change

^c One subject did not record the number of falls and was excluded from the recurrent falls analyses