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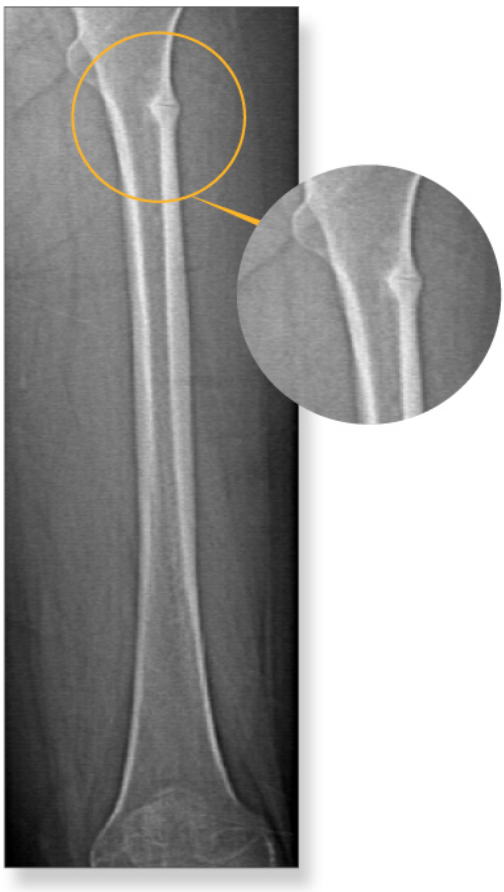

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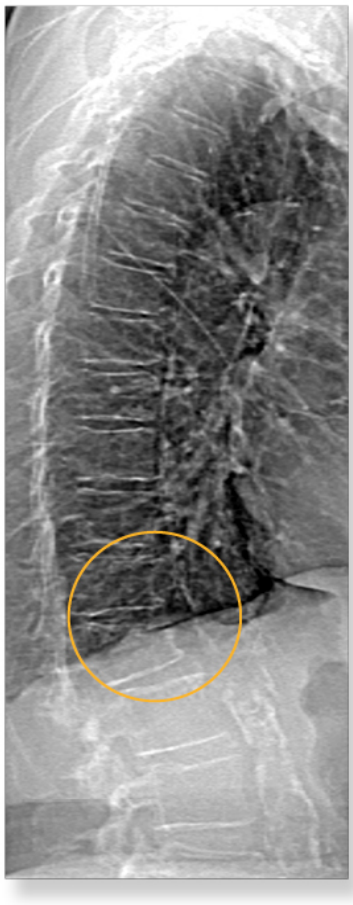

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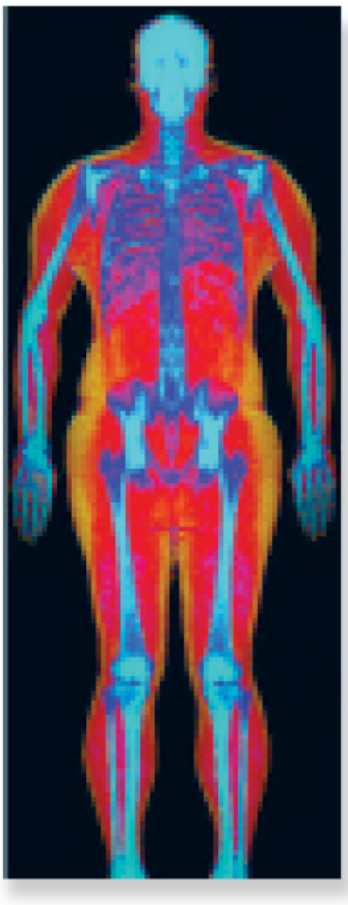

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Height Loss in Old Age and Fracture Risk Among Men in Late Life: A Prospective Cohort Study

Running Title: Height Loss and Fractures in Men

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Disclosures: The authors have nothing to disclose.

Data Availability Statement: MrOS data is available to the public via the 'MrOS Online' website (https://mrosonline.ucsf.edu/).

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ABSTRACT

To assess the association of height loss in old age with subsequent risk of hip and any clinical fracture in men late in life while accounting for the competing risk of mortality, we used data from 3,491 community-dwelling men (mean age 79.2 years). Height loss between baseline and follow-up (mean 7.0 years between examinations) was categorized as <1 cm (referent group), ≥1 to <2 cm, ≥2 to <3 cm, and ≥3 cm. Men were contacted every 4 months after the follow-up examination to ask about fractures (confirmed by radiographic reports) and ascertain vital status (deaths verified by death certificates). Competing risk methods were used to estimate absolute probabilities of fracture outcomes by height loss category and calculate adjusted risks of fracture outcomes by height loss. During an average of 7.8 years, 158 (4.5%) men experienced a hip fracture and 1,414 (40.5%) died before experiencing this event. The absolute 10-year probability of fracture events accounting for the competing risk of death increased with greater height loss. For example, the hip fracture probability was 2.7% (95% CI 1.9-3.8%) among men with height loss <1 cm increasing to 11.6% (95% CI 8.0-16.0%) among men with height loss ≥3 cm. After adjustment for demographics, fall history, multimorbidity, baseline height, weight change and femoral neck BMD and considering competing mortality risk, men with height loss ≥3 cm vs. <1 cm had a nearly 2-fold (subdistribution HR 1.94, 95% CI 1.06-3.55) higher risk of hip fracture and a 1.4-fold (subdistribution HR 1.42, 95% CI 1.05-1.91) increased risk of any clinical fracture. Height loss ≥3 cm in men during old age was associated with higher subsequent risk of clinical fractures, especially hip fractures, even after accounting for the competing risk of death and traditional skeletal and non-skeletal risk factors.

Keywords: height loss, fracture risk, older men

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INTRODUCTION

Height loss is associated with a higher risk of clinical fractures in middle-aged and older men.[1,2] However, findings of most previous studies are limited by inadequate control of potential confounding factors, a small number of fracture events and lack of consideration of the competing risk of mortality unrelated to fracture. Ignoring mortality may result in an overestimation of the effect of height loss on fracture risk because height loss is an independent predictor of death in older adults[1,3–5], making mortality a competing risk, especially late in life. While a few prior studies examining height loss in middle and old age and incident fracture risk have attempted to account for the competing risk of mortality, they have been limited by a short follow-up period of 2 years[6] or inadequate power to examine the association in men.[7] It is also uncertain whether any association of height loss in old age with subsequent fracture risk among men is independent of conventional skeletal and non-skeletal risk factors for fracture.

To determine the association of height loss in old age with subsequent risks of hip and any clinical fracture in men late in life while accounting for the competing risk of mortality and traditional fracture risk factors, we used data from 3,498 men enrolled in the Osteoporotic Fractures in Men (MrOS) study with measures of height loss and subsequent follow-up for fractures and mortality.

METHODS

Study Population

A total of 5,994 men ≥65 years old able to walk without the assistance of another person and without bilateral hip replacements were enrolled from 2000 to 2002 in the Osteoporotic Fractures in Men (MrOS) prospective cohort study.[8] Participants were recruited from population-

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based listings in six regions of the United States.[9] The institutional review board at each participating institution approved the study protocol and written informed consent was obtained from all participants. This analysis is limited to 3,491 men who attended both baseline and Year 7 (Y7) examinations with repeated height measurements and no missing covariates (Supplemental Figure 1).

Measurement of Height Loss

Height (with participant barefoot or in thin socks) was measured with a Harpenden stadiometer (calibrated every month) at both baseline and Y7 examinations (mean [SD] 7.0 [0.3] years between examinations). Participants were instructed to stand with their back, buttocks and both heels against the wall-mounted stadiometer. Height loss (cm) was calculated by subtracting baseline height from the Y7 height and expressed as an absolute value.

Ascertainment of Incident Clinical Fractures and Mortality

Participants in MrOS were contacted every 4 months after the baseline examination (over 98% of follow-up contacts were completed in active surviving participants) to ascertain vital status and ask about clinical fracture events. Self-reported fractures including hip fractures were confirmed by radiographic reports. For any self-reported spine fracture, radiographic reports and a copy of the community spinal imaging study (x-rays, CT and/or MRI) were obtained. Incident clinical vertebral fractures were confirmed by the study radiologist who used the semiquantitative method of Genant[10] to establish that the community imaging study showed a new deformity of a higher grade than was present in the same vertebra on study spine films performed at the baseline and Y5 examinations. Deaths were verified with death certificates. Participants in this analysis were followed up to a maximum of 10 years after the Y7 examination to ascertain incident outcomes of fracture and death. The primary fracture outcome

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of interest was hip fracture (mean [SD] follow-up time to event or censoring 7.8 [2.9] years); any clinical fracture (mean [SD] follow-up time to event or censoring 7.2 [3.2] years) was the main secondary outcome.

Other Measurements

Information regarding date of birth and self-reported race/ethnicity was collected at the baseline examination. At the Y7 examination, participants completed a questionnaire and were interviewed and asked about smoking status, falls in the past year and history of 12 selected medical conditions (see footnote, Table 1). A multimorbidity score was calculated (potential range 0-12) by summing up the number of self-reported medical conditions. Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE).[11] Poor energy was assessed by an answer of "no" to the question "Do you feel full of energy?" on the Geriatric Depression Scale.[12] Femoral neck bone mineral density (BMD) was measured with dual x-ray absorptiometry (DXA, QDR 4500W, Hologic, Inc., Bedford, MA) using standardized protocols.[13] Gait speed (time in seconds to walk 6 meters at usual pace [m/s]) and grip strength (Jamar handheld dynamometer) in kg were measured.

Body weight (in indoor clothing with shoes removed) was recorded with a scale (calibrated every month) at both the baseline and Y7 examinations; weight change was calculated by subtracting the baseline weight from the Y7 examination weight and expressed as a percentage of the baseline value.[14] New radiographic vertebral fractures between baseline and Year 5 (Y5) examinations were identified by a comparison of baseline and Y5 lateral thoracic and lumbar spine films (average 4.6 years between films). A single physician reader evaluated the baseline and Y5 images independently using the semi-quantitative (SQ) method of Genant[10] and was blinded to the order in which they were obtained. Incident radiographic vertebral

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fractures were defined as those with a change in SQ reading of ≥1 at a given vertebral level from the baseline to follow-up radiograph. For incident radiographic vertebral fracture with grade 1 severity, endplate depression was also required to distinguish fractured vertebrae from non-fracture deformities.[15]

Statistical Analysis

Height loss between the baseline and Y7 examination had a non-linear association with risk of fracture outcomes. In order to address non-linearity and facilitate interpretation of findings to the clinical practice setting, height loss was expressed as a categorical variable (<1 cm [referent group], ≥1 to <2 cm, ≥2 to <3 cm and ≥3 cm) in the analyses with categories based on findings from previous studies regarding clinically meaningful loss[1–5,7] and availability of sufficient numbers of participants and fractures in each category.

Characteristics of the 3,491 participants at Y7 across categories of height loss were compared using analysis of variance for normally distributed continuous variables; the chi square test or Fisher exact test was used for categorical data.

To estimate the absolute 10-year probability of a fracture outcome (i.e. hip fracture, any clinical fracture) during follow-up by height loss category, we used the cumulative incidence function that considers mortality as a competing risk and makes no assumptions regarding proportional hazards.[16]

To determine adjusted associations of height loss with risk of a fracture outcome, we used subdistribution hazards models proposed by Fine and Gray[17] that consider death as a competing risk. In unadjusted models, Fine and Gray models for clinical fracture exhibited time trends for some variables (i.e., age, BMD, multimorbidty and height loss). Findings were qualitatively similar for hip fracture. All time interactions had the effect of attenuation of the

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baseline effect over time, as expected when there is substantial mortality affecting the comparison group (survivors and deceased) at later time points. However, there were fewer time interactions (i.e., age and BMD) in the multivariate adjusted models. In particular, the time interaction for height loss (primary predictor of interest) was no longer present. Moreover, the effects noted for height loss were nearly identical in models including these age and BMD time interactions compared to models without these covariate time interactions. Therefore, simpler multivariate models are presented herein.

Associations were initially adjusted for age, race, and enrollment site alone (base model) and then further adjusted for traditional fracture risk factors including fall history, multimorbidity, baseline height, weight change and femoral neck bone mineral density (BMD). Subsequently, incident vertebral fracture was added to the multivariable model to determine whether any association between height loss and a given fracture outcome was explained by a higher prevalence of new vertebral fracture among men with greater height loss. Since height loss may reflect the shrinkage component of the frailty phenotype and phenotypic pre-frailty and frailty are risk factors for hip fracture, we also performed analyses adding additional components of the frailty phenotype (i.e. slowness [gait speed], weakness [grip strength], poor energy, low physical activity [PASE score]) one at a time to the multivariable model to determine the impact of adjustment for other frailty components on the association of height loss with hip fracture.

The Wald test[18] was used to determine if the addition of the height loss categorical variable to a Cox regression hip fracture model including traditional risk factors improved hazard prediction. Similarly, the Wald test was used to determine if the addition of the height loss categorical variable to a Fine and Gray hip fracture model including traditional risk factors and accounting for the competing risk of mortality enhanced cumulative incidence prediction.

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Finally, an analysis was performed using Fine and Gray subdistribution hazards models to determine the adjusted association of height loss with risk of clinical vertebral fracture.

RESULTS

Among the 3,491 men in the analytical cohort, mean (SD) participant age at the Y7 examination was 79.2 (5.2) years and mean (SD) height loss between baseline and Y7 examination was 1.5 (1.3) cm. Between baseline and Y7 examinations, a total of 1,262 men (36.2%) had height loss <1 cm, 1,448 (41.5%) had height loss ≥1 to <2 cm, 528 (15.1%) had height loss ≥2 to <3 cm and 253 (7.2%) had height loss ≥3 cm. Characteristics of the cohort overall and by category of height loss are shown in Table 1. In general, risk factors for fracture significantly varied across height loss categories with men with height loss ≥3 cm being at highest risk.

During a maximum follow-up of 10 years after the Y7 examination, 158 men (4.5%) experienced a hip fracture and 1,414 (40.5%) died prior to suffering a hip fracture. During this same time frame, 667 men (19.1%) experienced a clinical fracture including 108 (3% of overall cohort) men with clinical vertebral fracture and 1,187 (34.0%) died prior to experiencing a clinical fracture event.

Overall age-standardized incidence rates were 5.8 (95% CI 5.0-6.8) per 1000-person years for hip fracture, 26.4 (95% CI 24.5-28.5) per 1,000-person years for any clinical fracture and 54.8 (95% CI, 52.1-57.6) per 1,000 person-years for all-cause mortality (Table 1). Age-standardized rates of hip fracture, any clinical fracture and mortality increased with greater degree of height loss, increasing more than 6-fold for hip fracture and more than doubling for any fracture and mortality across height loss categories.

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After considering the competing risk of mortality, the absolute probability of hip fracture after Y7 increased with greater height loss between baseline and Y7 (Figure 1A). The probability at 5 years was 1.0% (95% CI: 0.5-1.6) among men with height loss <1 cm increasing up to 7.2% (95% CI 4.5-10.9) among men with height loss ≥3 cm. The risk gradient was not quite as steep at 10 years, but persisted with a hip fracture probability of 2.7% (95%CI: 1.9-3.8) among men with height loss <1 cm increasing up to 11.6% (95% CI 8.0-16.0) among men with height loss ≥3 cm. Similarly, the absolute probability of any clinical fracture after Y7 increased with greater height between baseline and Y7 (Figure 1B). The probability of clinical fracture at 5 years was 8.3% (95% CI: 6.9-9.9) among men with height loss <1 cm increasing up to 21.3% (95% CI 16.4-26.5) among men with height loss ≥3 cm, while the probability of clinical fracture at 10 years was 16.5% (95%CI: 14.5-18.6) among men with height loss <1 cm increasing up to 30.1% (95% CI 24.4-35.9) among men with height loss ≥3 cm.

After adjusting for age, race and enrollment site and considering the competing risk of death, hip fracture risk after Y7 increased with greater height loss between baseline and Y7 (Table 2). Compared with men with height loss <1 cm, the risk of hip fracture was 1.6-fold higher (HR 1.61 [95% CI 1.07-2.42]) among men with height loss ≥1 cm to <2 cm, nearly 2-fold higher (HR 1.95 [95% CI 1.20-3.16]) among men with height loss ≥2 cm to <3 cm and nearly 3.5-fold higher (HR 3.45 [95% CI 1.98-6.01]) among men with height loss ≥3 cm. The association was attenuated, but height loss ≥3 cm remained a risk factor for hip fracture after further accounting for multimorbidity, fall history, baseline height, weight change between baseline and Y7 and femoral neck BMD (HR [95% CI] 1.45 [0.96-2.17]) among men with height loss ≥1 cm to <2 cm, 1.49 [0.91-2.43] among men with height loss ≥2 cm to <3 cm and 1.94 [1.06-3.55] among men with height loss ≥3 cm). Additional adjustment for incident radiographic

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vertebral fracture between baseline and Y5 did not alter the multivariable association between height loss ≥3 cm between baseline and Y7 and subsequent risk of hip fracture. Similarly, the multivariable association of height loss ≥3 cm between baseline and Y7 with hip fracture risk after Y7 was not changed by the additional consideration of Y7 measures of gait speed, grip strength, physical activity level or poor energy.

A Wald test for a Cox regression model indicated improvement of hazard prediction with the addition of height loss to a model based on demographics, multimorbidity, fall history, baseline height, weight change and femoral neck BMD (χ^2=10.4, *p*-value 0.02). However, the improvement in cumulative incidence prediction with the addition of height loss to a competing risk model based on the same risk factors was not significant (χ^2=5.3, *p*-value 0.15).

Increasing height loss between baseline and Y7 was also associated with a higher risk of any clinical fracture after Y7 (Table 3) after consideration of demographics and the competing risk of mortality, but after further consideration of other traditional risk factors, the association of height loss ≥3 cm with risk of clinical fracture was modest in magnitude (HR [95% CI] 1.07 [0.89-1.29] for height loss ≥1 cm to <2 cm, 1.23 [0.97-1.57] for height loss ≥2 cm to <3 cm and 1.42 [1.05-1.91] for height loss ≥3 cm). After further consideration of new radiographic vertebral fracture between baseline and Y5, associations were slightly reduced in magnitude and no longer significant.

After adjustment for demographics and consideration of competing mortality risk, greater height loss between baseline and Y7 was associated with an increased risk of clinical vertebral fracture after Y7 (HR [95% CI] 1.49 [0.92-2.41] for height loss ≥1 cm to <2 cm, 1.84 [1.02-3.32] for height loss ≥2 cm to <3 cm and 2.20 [1.12-4.33] for height loss ≥3 cm) (Supplemental Table

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1). The association was somewhat attenuated and not significant after consideration of traditional risk factors.

DISCUSSION

In this prospective study of community-dwelling older men, height loss during old age was associated with higher subsequent risk of clinical fractures, including hip fractures. Men with a height loss ≥3 cm compared with men with height loss <1 cm during a seven-year period had a nearly 2-fold higher long term risk of hip fracture, even after accounting for the competing risk of death and traditional skeletal and non-skeletal risk factors for hip fracture. Of note, the association of height loss of ≥3 cm with hip fracture in our cohort did not appear to be explained by a greater likelihood of new vertebral fractures, markers of fall propensity or manifestations of physical frailty among men with greater height loss.

Our results are in general agreement with findings of previous prospective studies examining the association of height loss with fracture risk in middle-aged and older men. A study in 3,145 community dwelling older Chinese adults[1] including 1,562 men (mean age 71.8 years) reported that height loss ≥2 cm vs. <2 cm in 4 years in men was associated with a nearly 5-fold higher risk of hip fracture (but not all fractures) during a median follow-up period of 5.3 years. An investigation of 14,921 middle aged and older adults (6,424 men, mean age 59.3 years) enrolled in the EPIC-Norfolk cohort[2] with two measurements of height over an average of 3.7 years found that men with a height loss >1 cm/year compared with men with no height loss had a 4.5-fold increased risk of any fracture during a median follow-up of 7 years. Models for hip fracture showed a similar hazards ratio, but confidence intervals around the point estimate of the association overlapped 1.0. Neither of these studies considered the competing risk of death. Both

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were also limited by a small number of hip fracture events in men and lack of adjustment for traditional risk factors including DXA BMD and markers of fall propensity.

In our cohort of men in late life, the mortality incidence rate was 2-fold higher than the rate of clinical fracture and 9-fold higher than the rate of hip fracture, indicating that death was a major competitor to experiencing a hip fracture event during the 10-year follow-up period. Thus, our analyses used competing risk approaches. Despite accounting for the competing risk of death, men with height loss of ≥3 cm during a seven-year time period had a high (11.6%) 10-year absolute probability of hip fracture and nearly 2-fold higher risk of hip fracture after adjustment for traditional fracture risk factors. However, the association of height loss with hip fracture was non-linear; only 7% of the cohort had height loss of ≥3 cm and the competing risk of mortality was highest among this group. Thus, while the profound height loss in this small subset of older men markedly increased their fracture risk, the addition of height loss categories to a model accounting for traditional risk factors and the competing risk of death did not significantly improve cumulative incidence prediction for the broader population of older men. While a prior study[6] reported that accounting for the competing risk of death did not alter the association between recent height loss over 2 years and subsequent risk of hip fracture in 1,297 middle aged and older men, follow-up time for hip fracture was limited to only 2 years after the measurement of height loss. In addition, the analyses did not take into account potential confounders other than age and baseline height. More recently, a study[7] reported that greater height loss measured at the time of two DXA scans at least 1 year apart in 11,495 adults age 40 years and older was associated with an increase in risk of incident clinical fracture at all skeletal sites independent of clinical risk factors and competing mortality as assessed by the FRAX tool. However, power was insufficient to specifically determine the association in men as they

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comprised only 5% of the cohort.

We found that height loss ≥3 cm in old age was an independent predictor of risk of subsequent clinical fractures including hip fracture even after accounting for traditional clinical risk factors and hip BMD. Further adjustment for incident radiographic vertebral fractures occurring during a similar time period as the height loss did not alter the association of height loss ≥3 cm with hip fracture, though its association with any clinical fracture was no longer significant. Results of our study also suggest that height loss in old age is associated with increased risk of clinical vertebral fracture, but we did not have sufficient power to evaluate whether the association is independent of traditional risk factors. A previous study[3] in 3,124 late life women (mean age 84 years) at a Year 15 exam reported that height loss >5 cm vs. ≤5 cm between baseline and Year 15 exams was associated with a 1.5-fold increases in risk of any non-spine fracture including hip fracture during the subsequent 5 years after considering conventional lifestyle risk factors, hip BMD and incident radiographic vertebral fracture over the same time period as the height loss. However, unlike our study, this analysis did not account for the competing risk of mortality. While there is a general belief that height loss is associated with fracture risk because of underlying vertebral fractures, most age-related height loss is not attributable to vertebral fractures. Height loss may also result from age-related postural changes, increasing kyphosis, degeneration of intervertebral discs, weakening of muscle groups and non-osteoporotic spinal deformities. Height loss in late life may also be a proxy for non-skeletal risk factors for fracture, including poorer health status, propensity to fall and the frailty phenotype, especially the component of shrinking. However, the association of height loss ≥3 cm with fracture outcomes in our study persisted despite taking into account multimorbidity, history of falling, manifestations of physical frailty such as slowness and weight loss over the same time

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period as the height loss. Thus, substantial height loss in old age may be an indicator of subclinical illness or be related to the nature of fall descent or fall impact.

Our results have implications for fracture risk assessment in older men. Measurement of height is already routinely performed in the clinical practice setting as a part of the nursing intake to calculate body mass index, is accurate if performed properly using a wall-mounted stadiometer with the patient removing his/her shoes and is often available in the electronic medical record. Thus, height loss during old age appears to be a simple, inexpensive, and conveniently measured predictor of fracture risk, including hip fracture. While the proportion of older men who had substantial height loss in our cohort was less than 10%, these men were at high risk of hip fracture. Existing fracture risk assessment tools[19–21] do not include height measurements and all either ignore competing mortality risk[20,21] or rely solely on a general population mortality risk function that does not consider that many risk factors for fracture also increase risk of competing mortality.[19] Thus, our findings also suggest that future research should evaluate whether tools providing short-term and long-term estimates of fracture probability better identify late life individuals at high fracture risk by incorporating height measurements during old age and accounting for individual patient-based estimates of competing mortality risk. This work should include evaluating whether predictive validity of fracture prediction models incorporating height loss is superior to that of models based on traditional risk factors commonly assessed in the clinical practice setting such as age and BMD.

This study has several strengths. It was comprised of a large cohort of comprehensively characterized community-dwelling men with repeated height measurements, prospective long-term follow-up of vital status and fracture, and confirmation of incident fractures and deaths. However, this study also has a number of limitations. The cohort was predominantly older

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Caucasian community-dwelling men, so results may not be generalizable to other populations, such as late life adults residing in institutions. While random errors in measurement of height over time may have occurred in this study, these errors are likely to attenuate any association between height loss and fracture towards the null hypothesis of no association. Given the inaccuracies of height measurement that are likely present in clinical practice, the association may be less robust in this setting. Our study has an observational design. Thus, the possibility of residual confounding cannot be eliminated.

In conclusion, height loss ≥3 cm over seven years in men during old age was associated with higher subsequent risk of clinical fractures, especially hip fractures, even after accounting for the competing risk of death and traditional skeletal and non-skeletal risk factors. These findings support regular use of repeated measurements of height in the clinical practice setting to identify men in late life at increased risk of fractures, including hip fractures.

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Authors' roles:

Study concept and design: KEE, PMC, JAC

Data collection: KEE, PMC, JAC

Data analysis and interpretation: LL, KEE, JTS

Drafting manuscript: KEE

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Critical review and final approval of manuscript content: JTS, AMK, TNV, BCT, PMC, JAC, NEL, ARH, LL

Statistical Analysis: Dr. Langsetmo performed the statistical analyses and is independent of any commercial funder. She had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

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FIGURE LEGENDS

Figure 1A: Cumulative Absolute Probability of Hip Fracture by Height Loss Category

Figure 1B: Cumulative Absolute Probability of Any Clinical Fracture by Height Loss Category

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Table 1. Characteristics of 3,491 Men by Category of Height Loss

		Height Loss Category				
Characteristic*	Overall (N=3,491)	<1 cm (N=1,262)	≥1 to <2 cm (N=1,448)	≥2 to <3 cm (N=528)	≥3 cm (N=253)	P-value
Age, years, mean (SD)	79.2 (5.2)	77.8 (4.6)	79.1 (5.0)	80.8 (5.5)	82.7 (5.4)	<0.001
Caucasian race, n (%)	3,155 (90.4)	1,088 (86.2)	1,341 (92.6)	487(92.2)	239 (94.5)	<0.001
Ever smoker, n (%)	2,111 (60.5)	777 (61.6)	859 (59.3)	323 (61.2)	152 (60.1)	0.67
Multimorbidity score (0-12)†, mean (SD)	1.0 (1.1)	0.9 (1.0)	1.0 (1.1)	1.1 (1.1)	1.5 (1.3)	<0.001
Fall history, n (%)	673 (19.3)	205 (16.2)	281 (19.4)	112 (21.2)	75 (29.6)	<0.001
Poor energy, n (%)	1704 (49.0)	539 (42.9)	699 (48.4)	284 (54.1)	182 (72.8)	<0.001
PASE score, mean (SD)	132.2 (68.3)	140.2 (67.6)	134.8(67.9)	125.1 (65.5)	94.5 (66.4)	<0.001
Baseline height, cm, mean (SD)	174.7 (6.7)	174.5 (6.7)	175.0 (6.7)	174.2 (6.8)	174.2 (6.7)	0.07
Percent weight change, n (%)						<0.001
Weight loss ≥10%	707 (20.3)	210 (16.6)	280 (19.3)	147 (27.8)	70 (27.7)	
Weight loss 5% to <10%	369 (10.6)	55 (4.4)	143 (9.9)	90 (17.1)	81 (32.0)	
Stable weight (loss or gain <5%)	2107 (60.4)	837 (66.3)	908 (62.7)	267 (50.6)	95 (37.6)	

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Weight gain ≥5%	308 (8.8)	160 (12.7)	117 (8.1)	24 (4.6)	7 (2.8)	
Femoral neck BMD, g/cm^2, mean (SD)	0.77 (0.13)	0.79 (0.13)	0.77 (0.13)	0.75 (0.13)	0.71 (0.15)	<0.001
Gait speed, m/s, mean (SD)	1.13 (0.23)	1.17 (2.1)	1.15 (0.22)	1.06 (0.24)	0.91 (0.25)	<0.001
Grip strength, kg, mean (SD)	38.9 (8.5)	40.6 (7.9)	39.2 (8.3)	37.0 (8.6)	32.(8.7)	<0.001
New radiographic vertebral fracture, n (%)	137 (3.9)	17 (1.4)	40 (2.8)	43 (8.1)	37 (14.6)	<0.001
Incidence rate (95% CI) per 1,000 person-years‡						
Hip fracture	5.8 (5.0-6.8)	3.4 (2.2-4.5)	5.6 (4.3-7.0)	6.8 (4.3-9.2)	22.3 (11.0-33.5)	<0.001
Clinical fracture	26.4 (24.5-28.5)	21.8 (18.7-24.8)	25.2 (22.3-28.2)	31.2 (25.5-36.9)	48.6 (34.6-62.5)	<0.001
All-cause mortality	54. 8 (52.1-57.6)	45.1 (40.8-49.3)	52.5 (48.5-56.5)	62.5 (55.2-69.9)	105.9 (86.1-125.7)	<0.001

Abbreviations: PASE, Physical Activity Scale for the Elderly; BMD, bone mineral density

*All characteristics measured at Y7 except height (baseline), weight change (which is between baseline and Y7) and new radiographic vertebral fracture (which is between baseline and Y5)

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†Multimorbid conditions include stroke, diabetes, Parkinsonism, coronary heart disease [myocardial infarction, angina], congestive heart failure, chronic obstructive pulmonary disease, non-skin cancer, depression, dementia, rheumatoid arthritis, liver disease, and renal disease.

‡adjusted for age

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Table 2. Subdistribution Models for Association of Height Loss with Hip Fracture

	Hazard Ratio (95% CI)			
Hip fracture (N= 158)	Height Loss <1 cm (N= 1,262)	Height Loss ≥1 cm to <2 cm (N= 1,448)	Height Loss ≥2 cm to <3 cm (N= 528)	Height Loss ≥3 cm (N= 253)
Base model*	1.00 (referent)	1.61 (1.07-2.42)	1.95 (1.20-3.16)	3.45 (1.98-6.01)
MV model†	1.00 (referent)	1.45 (0.96-2.17)	1.49 (0.91-2.43)	1.94 (1.06-3.55)
MV Model + new vertebral fracture	1.00 (referent)	1.45 (0.96-2.18)	1.50 (0.92-2.46)	1.98 (1.07-3.65)
MV model + poor energy (N=3477)	1.00 (referent)	1.44 (0.96-2.17)	1.49 (0.91-2.43)	1.92 (1.05-3.51)
MV model + PASE score (N=3482)	1.00 (referent)	1.45 (0.96-2.18)	1.49 (0.91-2.43)	1.90 (1.04-3.50)
MV model + gait speed (N=3467)	1.00 (referent)	1.43 (0.95-2.15)	1.44 (0.88-2.38)	1.91 (1.02-3.56)
MV model + grip strength (N=3404)	1.00 (referent)	1.48 (0.98-2.25)	1.44 (0.87-2.39)	1.95 (1.05-3.63)

Abbreviations: MV, multivariable

*adjusted for age, race, and enrollment site

†base model further adjusted for multimorbidity, fall history, baseline height, weight change and femoral neck BMD

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Table 3. Subdistribution Models for Association of Height Loss with Any Clinical Fracture

	Hazard Ratio (95% CI)			
Clinical fracture (N= 667)	Height Loss <1 cm (N= 1,262)	Height Loss ≥1 cm to <2 cm (N= 1,448)	Height Loss ≥2 cm to <3 cm (N= 528)	Height Loss ≥3 cm (N= 253)
Base model*	1.00 (referent)	1.13 (0.94-1.35)	1.37 (1.09-1.74)	1.73 (1.30-2.32)
MV model†	1.00 (referent)	1.07 (0.89-1.29)	1.23 (0.97-1.57)	1.42 (1.05-1.91)
MV Model + new vertebral fracture	1.00 (referent)	1.06 (0.88-1.27)	1.18 (0.93-1.49)	1.31 (0.97-1.77)

Abbreviations: MV, multivariable

*adjusted for age, race, and enrollment site

†base model further adjusted for multimorbidity, fall history, baseline height, weight change and femoral neck BMD

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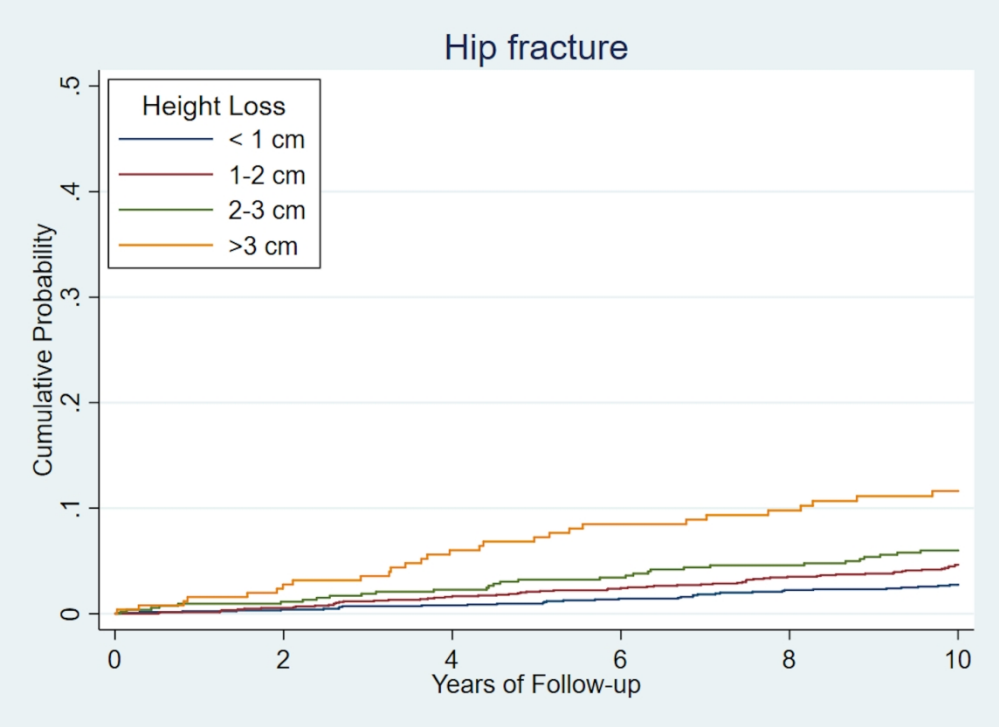

Cumulative Absolute Probability of Hip Fracture by Height Loss Category

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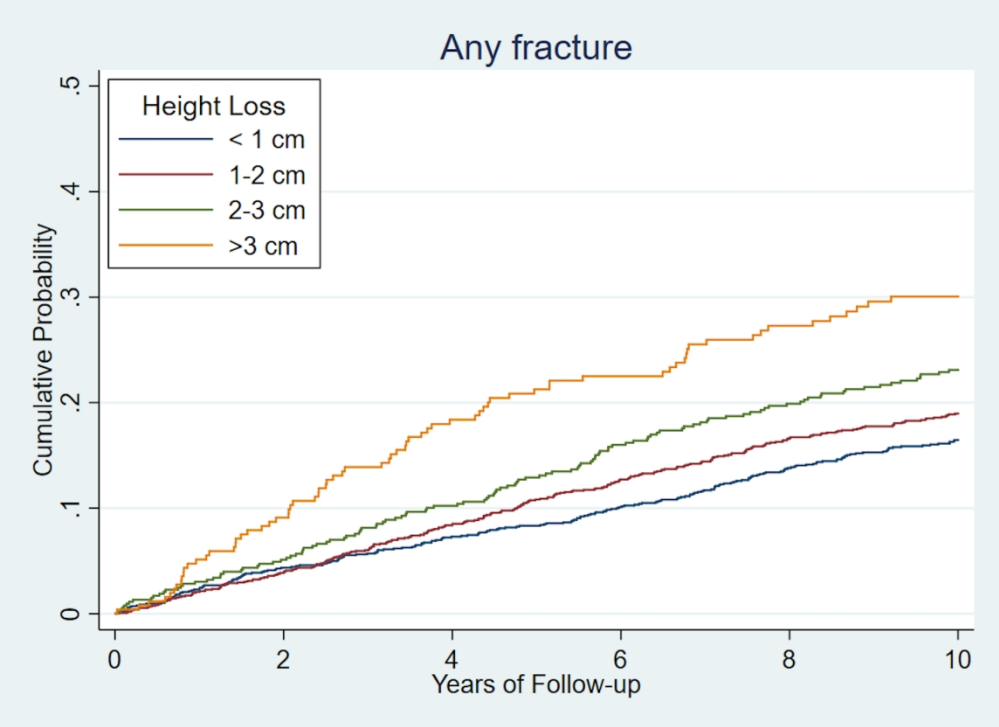

Cumulative Absolute Probability of Any Clinical Fracture by Height Loss Category

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