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# **Low calcaneal bone mineral density and the risk of distal forearm fracture in women and men: A population-based case-control study**

Isam Atroshi<sup>a</sup>, Fredrik Åhlander<sup>b</sup>, Mats Billsten<sup>c</sup>, Henrik G. Ahlberg<sup>d</sup>,

Dan Mellström<sup>e</sup>, Claes Ohlsson<sup>f</sup>, Östen Ljunggren<sup>g</sup>, Magnus K. Karlsson<sup>h</sup>

<sup>a</sup> Associate professor in orthopedics, Department of Clinical Sciences, Lund University, Lund, Sweden, and Department of Orthopedics, Hässleholm and Kristianstad Hospitals, SE-28125 Hässleholm, Sweden. Tel: +46 443091279; E-mail: [Isam.Atroshi@skane.se](mailto:Isam.Atroshi@skane.se)

<sup>b</sup> Specialist, Department of Orthopedics, Hässleholm Hospital, Hässleholm, Sweden.

<sup>c</sup> Consultant, Department of Orthopedics, Hässleholm Hospital, Hässleholm, Sweden.

<sup>d</sup> Consultant in orthopedics, Clinical and Molecular Osteoporosis Research Unit, Department of Clinical Sciences and Orthopedics, Lund University, Lund, Sweden.

<sup>e</sup> Professor and consultant in geriatrics, Department of Geriatrics, Gothenburg University, Gothenburg, Sweden.

<sup>f</sup> Professor and consultant in internal medicine, Department of Internal Medicine, Gothenburg University, Gothenburg, Sweden.

<sup>g</sup> Professor and consultant in internal medicine, Department of Medical Sciences, Uppsala University Hospital, Uppsala, Sweden.

<sup>h</sup> Professor and consultant in orthopedics, Clinical and Molecular Osteoporosis Research Unit, Department of Clinical Sciences and Orthopedics, Lund University, Lund, Sweden.

Corresponding author: Isam Atroshi

## ABSTRACT

**Objective:** We used dual X-ray absorptiometry (DXA) to measure calcaneal bone mineral density (BMD) and estimate the prevalence of osteoporosis in a population with distal forearm fracture and a normative cohort.

**Methods:** Patients 20 to 80 years of age with distal forearm fracture treated at one emergency hospital during two consecutive years were invited to calcaneal BMD measurement; 270 women (81%) and 64 men (73%) participated. A DXA heel scanner estimated BMD ( $\text{g}/\text{cm}^2$ ) and T-scores. Osteoporosis was defined as T-score  $\leq -2.5$  SD. Of the fracture cohort, 254 women aged 40-80 years and 27 men aged 60-80 years were compared with population-based control cohorts comprising 171 women in the age groups 50, 60, 70 and 80 years and 75 men in the age groups 60, 70, and 80 years.

**Results:** In the fracture population no woman below 40 years or man below 60 years of age had osteoporosis. In women aged 40-80 years the prevalence of osteoporosis in the distal forearm fracture cohort was 34% and in the population-based controls was 25%; the age-adjusted prevalence ratio (PR) was 1.32 (95% CI 1.00-1.76). In the subgroup of women 60-80 years the age-adjusted prevalence ratio of osteoporosis was 1.28 (95% CI 0.95-1.71). In men aged 60-80 years the prevalence of osteoporosis in the fracture cohort was 44% and in the population-based controls was 8% (PR 6.31, 95% CI 2.78-14.4). The age-adjusted odds ratio for fracture associated with a 1-SD reduction in calcaneal BMD was in women aged 40-80 years 1.4 (95% CI 1.1-1.8), in the subgroup of women 60-80 years 1.2 (95% CI 0.95-1.6), and in men 60-80 years 2.6 (95% CI 1.7-4.1). Among those aged 60-80 years the area under the ROC curve was in women 0.56 (95% CI 0.49-0.63) and in men 0.80 (95% CI 0.70-0.80).

**Conclusions:** The age-adjusted prevalence of osteoporosis based on calcaneal BMD is higher in individuals with distal forearm fracture than in population-based controls. BMD impairment is associated with increased odds ratio for forearm fracture in both women and men but the differences between cases and controls are more pronounced in men than in women, which may have implications in fracture prevention.

## **Introduction**

Osteoporosis, diagnosed as a bone mineral density (BMD) T-score of  $-2.5$  or lower measured at the hip or lumbar spine with a total body scanner [1], is considered a strong predictor of fragility fractures [2], the most common of which is the distal forearm fracture. The increasing numbers of fragility fractures [3] have forced the implementation of new prevention strategies. One advocated strategy to reduce the incidence of fractures is to identify individuals with osteoporosis for prophylactic treatment [4]. As a distal forearm fracture usually precedes hip fracture [5], sustaining this fracture has been accepted as indication to perform BMD measurement. A low BMD would constitute indication for prophylactic drug treatment, as randomized trials have shown that drug treatment in individuals with osteoporosis reduces fracture risk [4].

The prevalence of osteoporosis in individuals with a distal forearm fracture has been predominantly studied in women based on lumbar spine and hip BMD measurements using dual energy X-ray absorptiometry (DXA) total body scanner, but these studies, mostly with small sample sizes, have yielded disparate results [6-9]. No studies have specifically focused on BMD in men with distal forearm fracture.

Because access to total body scanners is limited due to their high costs and need for stationary scanning facilities and special trained technicians, portable DXA devices for BMD measurement are being increasingly used. Portable DXA devices for the calcaneus have reportedly shown good sensitivity and specificity in diagnosing osteoporosis [10]. It is unclear whether the age-and gender-specific prevalence of osteoporosis is similar when BMD is measured in the lumbar spine, hip or calcaneus.

This study aimed to determine the prevalence of osteoporosis in a distal forearm fracture cohort and a population-based control cohort based on DXA-measured calcaneal BMD and to investigate the relationship between calcaneal BMD impairment and the occurrence of distal forearm fracture in women and men.

## **Materials and methods**

### ***Distal forearm fracture cohort***

All patients 20 to 80 years of age treated for an acute distal forearm fracture at the only emergency department that serves the southern Swedish region of northeastern Scania (population 170,000), between April 1, 2000 and March 31, 2002 were eligible. All patients, except those with severe medical illness, cognitive disorder or residence outside the study

region, were invited to calcaneal BMD measurement ( $\text{g}/\text{cm}^2$ ). Those who missed or declined BMD measurement were reinvited after one year and again after two to three years to a delayed BMD measurement.

During the 2-year period, 333 women and 88 men were eligible. Of these, 270 women and 64 men accepted BMD measurement (participation rate 81% and 73%, respectively). The median time from fracture to BMD measurement was 11 (range 0-36) months in women and 11 (2-36) months in men, with measurement done within 1 year after fracture in 199 (59.6%), from 1 to 2 years in 89 (26.6%) and after 2 years in 46 (13.8%). The type of trauma among 16 women below 40 years was fall from standing height in 6, fall from unspecified higher level in 1, sports-related injury in 8, and traffic accident in 1, and among the 254 women 40 years or older the corresponding numbers were 189, 48, 13 and 2, respectively (unknown in 2 women). The type of trauma among 37 men below 60 years was same-level fall in 9, higher-level fall in 18, sport-related injury in 7, and traffic accident in 3 and among 27 men 60 years or older the corresponding numbers were 23, 3, 0 and 1, respectively.

Among the participants examined current bisphosphonate treatment was reported by 25 women (18 aged 60-80 years), of whom 12 were measured within 4 months of fracture, 5 within 1 year, and 8 after 1 year. Hormone therapy (estrogen) was reported by 9 women (6 aged 60-80), of whom 3 were measured within 4 months, 2 within 1 year and 4 after 1 year of fracture. Intake of Calcium supplements (with or without vitamin D) was reported by 31 women (18 aged 60-80), of whom 14 were measured after 1 year of fracture. None of the men had bisphosphonate treatment. Intake of Calcium supplements was reported by 3 men (2 aged 60-80), of whom 1 was measured after 1 year of fracture.

All patients were ambulatory and none was wheelchair-bound.

### ***Population-based control cohorts***

The control cohorts in this study were derived from population-based cohorts, also from the region of Scania, that participated in the Malmö-Sjöbo study described previously [11].

*Women controls:* In the Malmö-Sjöbo study 247 women, born 1948, 1938, 1928 and 1918, who had been randomly selected from the national population records of the city of Malmö were invited in 1998 to undergo examinations that included calcaneal BMD measurement. Of those women invited, 171 (69%) attended, of whom 39 (23%) reported history of a previous fragility fracture. These 171 women aged 50, 60, 70 or 80 years at calcaneal BMD measurement constituted the control cohort in the present study.

*Men controls:* In the Malmö-Sjöbo study 127 men, born 1938, 1928 and 1918, who had been randomly selected from the national population records of Malmö were similarly invited

in 1998 to undergo calcaneal BMD measurement; 75 (59%) attended, of whom 4 (5.3%) reported a previous fragility fracture. These 75 men aged 60, 70 or 80 years at calcaneal BMD measurement constituted the control cohort in the present study.

### ***BMD measurement***

Measurements of calcaneal BMD ( $\text{g}/\text{cm}^2$ ) in the patients and controls were done with DXA using the Calscan densitometer (Demetech, Solna, Sweden) throughout the study. This portable device combines DXA with measurement of heel thickness using laser technique [10]. The measurements were done at the right heel in 207 (62%) and the left heel in 127 (38%) of the patients by three trained examiners and the right heel in all controls by one trained examiner. The normative population used for the gender-specific T-score calculations (women aged 18-27 and men aged 20-29 years) was derived from normative database of Caucasians provided by the Calscan software (993 healthy Caucasian women aged 15-85 years and 459 healthy Caucasian men aged 19-85 years from Southern Sweden) [12]. The equipment had a precision of 1.2% in that population [12]. The WHO definitions of osteopenia (BMD T-score  $-1$  to  $>-2.5$ ) and osteoporosis (BMD T-score  $\leq -2.5$ ) were applied to the calcaneal BMD, with the knowledge that the original definitions were based on BMD measured with total body DXA scanners in postmenopausal women [1]. Body height and weight were measured.

### ***Statistical analysis***

Data are presented as mean and standard deviation (SD) or mean with 95% confidence interval (95% CI). The prevalence of osteoporosis and osteopenia is reported as gender and age-specific rate. The fracture subcohorts of women aged 40-80 years, and of women and men aged 60-80 years were compared with the population-based normative cohorts of women aged 50, 60, 70 and 80 years, and of women and men aged 60, 70 and 80 years, respectively. Comparisons of calcaneal BMD and T-scores were done with analysis of covariance (ANCOVA) using age at BMD measurement as a covariate. Analyses adjusting for body mass index gave similar results. The age-adjusted prevalence ratios of osteoporosis and of osteopenia in the fracture cases and the population-based controls were calculated by robust-variance Cox regression analysis. Receiver operating characteristic (ROC) analyses were performed to assess the degree to which calcaneal BMD discriminated individuals with distal forearm fracture from the individuals in the population-based cohort, with calcaneal BMD expressed as Z-scores to account for age. The area under the ROC curve (AUC) and 95% CI was calculated. The odds ratio (OR) of having sustained a distal forearm fracture with 1-SD BMD impairment was calculated from logistic regressions based on Z-

scores and adjusting for age. To assess whether the differences in time from fracture to BMD measurement may have influenced BMD values in the fracture population, we performed a linear regression analysis to determine the age-adjusted association between BMD and time from fracture to measurement ( $\leq 1$  year, 1-2 years, and  $> 2$  years), showing no significant difference in age-adjusted BMD between the groups (regression coefficient for women,  $-0.002$ ,  $P=0.71$ , and for men  $0.018$ ,  $P=0.57$ ). All statistical tests were two-sided and a  $P$  value of  $<0.05$  was considered a statistical significant difference. Informed consent was obtained from all participants and the study was approved by the Ethics Committee of Lund University and performed according to the Helsinki declaration.

## **Results**

### ***Prevalence of osteoporosis***

In the distal forearm fracture cohort calcaneal BMD impairment increased with age, with osteoporosis found in half of the women and men aged 71 to 80 years but in no women below 40 years and in no men below 60 years (Table 1). The median time from fracture to BMD measurement in women with normal BMD was 11 months, osteopenia 11 months and osteoporosis 12 months and the corresponding intervals in men were 15, 13 and 14 months respectively.

In the normative cohorts, osteoporosis was uncommon among women aged 50 and 60 years but was present in one third of those aged 70 years and in more than half of those aged 80 years, whereas in men osteoporosis was uncommon (Table 1).

### ***Comparison of the fracture and normative cohorts***

In women aged 40-80 years the mean BMD and T-score were significantly lower in the fracture than in the control population; the age-adjusted mean difference for BMD was  $-0.103$  (95% CI  $-0.117$ - $-0.089$ ,  $P<0.001$ ) and for T-score was  $-0.30$  (95% CI  $-0.48$ - $-0.12$ ,  $P=0.001$ ). The prevalence of osteoporosis was 34% in the fracture women and 25% in the controls; the age-adjusted prevalence ratio (PR) was 1.32 (95% CI 1.00-1.76,  $P=0.053$ ). The prevalence of osteopenia or osteoporosis in the fracture and control women was 94% and 75%, respectively, for an age-adjusted PR of 1.23 (95% CI 1.12-1.34,  $P<0.001$ ). Of the 25 women receiving bisphosphonate therapy 13 had osteoporosis and 12 had osteopenia. Of the 9 women receiving hormone therapy 2 had osteoporosis and 5 had osteopenia and of the 31 women receiving calcium supplements 9 had osteoporosis and 22 had osteopenia.

In the subgroup of women aged 60-80 years, the age adjusted mean difference in BMD was significant (lower in the fracture women) but the difference in age-adjusted mean T-score did not reach statistical significance and the age-adjusted prevalence ratio of osteoporosis was 1.28 (95% CI 0.95-1.71,  $P=0.10$ ) (Table 2). Excluding the 37 control women aged 60-80 years with history of a previous fragility fracture (16 with osteoporosis and 17 with osteopenia) resulted in an age-adjusted mean difference in BMD of  $-0.103$  (95% CI  $-0.121$ - $-0.068$ ,  $P<0.001$ ) and in T-score of  $-0.31$  (95% CI  $-0.53$ - $-0.08$ ,  $P=0.007$ ).

Among men aged 60-80 years the age-adjusted mean differences in BMD and T-scores were significant (lower in the fracture men by a mean of  $0.2 \text{ g/cm}^2$  and  $1.6$  respectively) and the prevalence of osteoporosis was 44% versus 8%, for an age-adjusted prevalence ratio of 6.31 (95% CI 2.78-14.4,  $P<0.001$ ). Excluding the 4 control men with history of a previous fragility fracture (1 with osteoporosis and 2 with osteopenia) did not substantially alter the results. Of the 3 men receiving calcium supplements 1 had osteoporosis and 2 had osteopenia.

The age-adjusted OR to have sustained a distal forearm fracture with 1-SD impairment of calcaneal BMD was in women aged 40-80 years 1.4 (95% CI 1.1-1.8,  $P=0.002$ ), in women aged 60-80 years 1.2 (95% CI 0.95-1.6,  $P=0.11$ ) and in men aged 60-80 years 2.6 (95% CI 1.7-4.1,  $P<0.001$ ).

The ROC analysis showed that calcaneal BMD could discriminate between the fracture and control populations with higher discrimination shown among men than among women. The AUC in women aged 40-80 years was 0.58 (95% CI 0.52-0.64,  $P=0.005$ ), in the subgroup of women aged 60-80 years was 0.56 (95% CI 0.49-0.63,  $P=0.067$ ), and in men aged 60-80 years was 0.80 (95% CI 0.70-0.90,  $P<0.001$ ).

## **Discussion**

This study is one of the largest population-based studies measuring calcaneal BMD with DXA in women following distal forearm fracture and one of the few studies that included men. The results show that 40% of women and men above 60 years of age with distal forearm fracture have osteoporosis. Osteopenia but not osteoporosis is common among individuals with distal forearm fracture below age 60 years. Most fractures occurred in the larger group with osteopenia even though the relative risk is higher in the smaller group of individuals with osteoporosis, a finding similar to previous reports using lumbar spine or hip BMD in fracture prediction [1]. Although the WHO definition of osteoporosis is based on DXA-measured hip,



spine and distal forearm BMD, the findings from a previous study of DXA-measured calcaneal BMD also supported the use of the WHO T-score thresholds [10].

The current study infers that calcaneal BMD seems to have better predictive ability for distal forearm fracture in men than in women. The prevalence ratio was substantially higher in men than in women, because among the controls osteoporosis was much less common in men than women whereas among the fracture population aged 60 years or older it was somewhat higher in men. Considering that distal forearm fracture has been suggested to be a better predictor of hip fracture in men than in women [13], we speculate that when trying to identify individuals with high risk of future hip fracture, BMD measurement may be of higher value in men than in women. The possible preventive role of implementing wider osteoporosis treatment in men with distal forearm fracture needs to be evaluated in large prospective studies and studies using BMD measurements at other sites. However, in this context, it is unlikely that BMD measurement at other sites would yield substantially different results.

It is known that men with hip fracture have a higher proportion of secondary osteoporosis and that they are more prone to alcohol excess [14]. We therefore speculate that the larger discrepancy in men than in women when comparing the forearm fracture cohort with the controls could also be based on similar factors.

In women with distal forearm fracture the prevalence of osteoporosis has been studied predominantly with BMD measurements at the spine or hip. In an English cohort of 106 women, mean age 66 (37-89) years, the prevalence of osteoporosis was 21% (spine), 42% (hip), and 50% (either site) [6], and in a Spanish cohort of 58 women, mean age 66 (45-80) years, the prevalence was 47% (spine) and 19% (hip) [7]. In a Dutch cohort of 94 women, mean age 69 (55-79) years, osteoporosis prevalence (spine or hip) was 51% [8], and in an Irish cohort of 100 women, mean age 68 (60-86) years, it was 68% [9]. These somewhat diverging rates can be compared with osteoporosis prevalence in our study, based on DXA-measured calcaneal BMD, of 34% in 254 women with a mean age of 66 (40-80) years. Thus, it seems that heel DXA scan provides osteoporosis prevalence rates similar to those found by a number of other studies that measured BMD at the hip or spine by total body scanner. An English study used calcaneal DXA (Lunar PIXI equipment) to examine 78 of the 207 women who had presented with low-trauma distal forearm fracture to a hospital's fracture clinic (38% participation), showing in this group with mean age of 71 (40-80) years a mean BMD of 0.40 g/cm<sup>2</sup> and osteoporosis prevalence (using manufacturer's criteria of calcaneal BMD T-score of -1.6) of 42% [15].

In two previous studies, a significantly higher prevalence of osteoporosis in women with distal forearm fracture compared with age-matched women without fracture was found only among those aged 65 years or younger [6,7]. Results of such comparisons could be influenced in different studies by factors such as the size of the fracture cohort, participation rate, age ranges included, sites measured, or type of control cohorts (normative population or age-matched women with no fracture). We used population-based normative cohorts that among women included a substantial number with previous fragility fracture. This may explain why calcaneal BMD measurement showed low discrimination between the fracture and control populations in women 60 to 80 years of age. However, for the specific purpose of evaluating distal forearm fracture risk among women and men, it should be appropriate to use comparable population-based controls rather than select only healthy persons without any previous fragility fracture.

A study evaluated the predictive ability of different BMD measurements in four female fracture cohorts with distal forearm fracture (78 patients, mean age 68) and hip, proximal humerus and vertebral fractures (approximately 100 patients, mean age 71) and a normative cohort (500 postmenopausal women aged 55-80, mean 67 years) [16]. In predicting a distal forearm fracture, the OR with 1-SD decrease in hip BMD was 1.7 and in calcaneal BMD (4 different calcaneal quantitative ultrasound devices) ranged from 1.7 to 2.0. In a European study, the AUC for calcaneal ultrasound in predicting hip fracture was 0.66 [17]. A recent analysis of nine large population-based studies including mainly women reported that, in predicting hip fracture, the mean AUC for hip BMD was 0.62 [18]. These results can be compared to OR of 1.4 and AUC of 0.58 in predicting distal forearm fracture in women in our study, indicating that calcaneal BMD measurement appears to have predictive ability for osteoporosis-related fractures that does not substantially differ from that of lumbar spine and hip BMD. In several studies calcaneal BMD has been measured by other methods than DXA, such as ultrasound, with similar results [16,17]. Estimation of distal forearm fracture risk can also be done by measuring BMD at the distal forearm with portable DXA densitometer [19]

In our study, the comparisons involved women from age 40 years and men from age 60 years. Thus the sample size for the fracture predictive ability was small for men, which influenced the precision of the prevalence ratio for osteoporosis, with a wider confidence interval. However, osteoporosis was not found in the age groups for which controls were not available.

The study strengths are the inclusion of most individuals with distal forearm fracture from a defined general population over two years enhancing generalizability, high participation rate

(81% of all women and 73% of all men with a distal forearm fracture), and inclusion of a population-based control cohort from the same region. The study has limitations. We used the young normative database included in the Calscan software for T-score calculations. However, the database includes Caucasians measured in southern Sweden, suggesting a representative young control population. Another limitation is the median period of 11 months between fracture and BMD measurements but the time in individuals with normal and those with impaired BMD only differed by 1 to 2 months and no age-adjusted differences in BMD were found between those measured after different time intervals. However, because this comparison involves averages, differences in BMD could have been found if a pair-wise analysis of BMD between the time of fracture and 11 months later were performed. Therefore, it is still possible that, for a proportion of patients, the BMD value at the time of the forearm fracture was different from that at BMD measurement. Also, a number of patients have undergone anti-osteoporosis treatment that will increase BMD, as it has been shown that BMD will significantly increase following one year of alendronate treatment [20]. However, because among the women receiving treatment the prevalence of osteoporosis and of osteopenia was similar to that for the whole woman fracture population, this factor could not have substantially influenced the prevalence ratios.

Another limitation is that BMD was measured in the left calcaneus in half the fracture cohort but in the entire control cohort; however, studies have shown that discrepancy in BMD between the right and left calcaneus has no clinical relevance [12,21]. It should also be emphasized that fracture risk can be influenced by other factors not assessed in the present study, such as activity levels, motor function, neurological disorders and arthritis that may affect BMD or the risk of falls [22].

Calcaneal BMD measurement showed significantly lower values in individuals with a distal forearm fracture than in population-based controls, and in the age interval of 60 to 80 years the differences were more pronounced among men than among women, which may have implications in fracture prevention. Portable scanners may be useful in detecting persons at high risk of future fracture and in this respect more attention needs to be directed to men with forearm fracture.

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**Table 1** Calcaneal bone mineral density (BMD) stratified according to age

Age group (y)	Fracture <i>N</i>	Examined <i>N</i>	BMD (g/cm <sup>2</sup> ) mean (SD)	Osteopenia <i>N</i> (%)	Osteoporosis <i>N</i> (%)
Fracture women					
≤ 40	24	17	0.432 (0.05)	7 (41)	0 (0)
41-50	18	16	0.399 (0.05)	11 (69)	1 (6.3)
51-60	79	67	0.362 (0.05)	48 (72)	15 (22)
61-70	101	77	0.346 (0.06)	48 (62)	25 (33)
71-80	111	93	0.316 (0.06)	45 (48)	46 (50)
Control women					
50		53	0.507 (0.10)	30 (57)	4 (7.6)
60		41	0.471 (0.08)	25 (61)	3 (7.3)
70		41	0.438 (0.09)	20 (49)	14 (34)
80		36	0.376 (0.10)	12 (33)	21 (58)
Fracture men					
≤ 50	33	24	0.513 (0.10)	11 (46)	0 (0)
51-60	23	13	0.472 (0.05)	9 (69)	0 (0)
61-70	19	15	0.414 (0.13)	4 (27)	6 (40)
71-80	13	12	0.352 (0.07)	6 (50)	6 (50)
Control men					
60		21	0.611 (0.10)	9 (43)	0 (0)
70		30	0.582 (0.10)	12 (40)	2 (6.7)
80		24	0.564 (0.13)	8 (33)	4 (17)

The WHO definition of osteopenia (T-score -1 to >-2.5) and osteoporosis (T-score ≤-2.5) applied.

**Table 2** Calcaneal bone mineral density (BMD), T-scores, and prevalence of osteoporosis and osteopenia in the fracture and population-based control women and men aged 60-80 years

	Fracture	Control	Age-adjusted mean difference <sup>a</sup> or prevalence ratio <sup>b</sup> (95% CI)	<i>p</i> -value
<b>Women 60-80 y</b>	<i>N</i> = 179	<i>N</i> = 118		
Age	71 (6)	70 (8)		0.18
BMI	26.7 (4.2)	26.7 (4.7)		0.92
BMD	0.332 (0.06)	0.431 (0.09)	-0.094 (-0.111, -0.077)	<0.001
T-score	-2.25 (0.8)	-2.0 (1.2)	-0.19 (-0.40, 0.03)	0.084
Osteoporosis, <i>N</i> (%)	74 (41)	38 (32)	1.28 (0.95, 1.71)	0.10
Osteopenia/osteoporosis, <i>N</i> (%)	173 (97)	95 (81)	1.19 (1.09, 1.30)	<0.001
<b>Men 60-80 y</b>	<i>N</i> = 27	<i>N</i> = 75		
Age	69 (6)	70 (8)		0.43
BMI	26.1 (4.3)	25.7 (3.6)		0.65
BMD	0.386 (0.11)	0.584 (0.11)	-0.202 (-0.250, -0.154)	<0.001
T-score	-2.13 (1.4)	-0.62 (1.4)	-1.6 (-2.2, -0.96)	<0.001
Osteoporosis, <i>N</i> (%)	12 (44)	6 (8)	6.31 (2.78, 14.4)	<0.001
Osteopenia/osteoporosis, <i>N</i> (%)	22 (82)	35 (47)	1.78 (1.33, 2.40)	<0.001

Values shown as mean (SD) unless specified otherwise

<sup>a</sup>BMD and T-scores using analysis of covariance (ANCOVA) adjusting for age at BMD measurement

<sup>b</sup>Osteoporosis and osteopenia/osteoporosis (see footnote in Table 1 for definitions) using a Cox regression model