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Body Mass Index, Waist Circumference, and Risk of Incident Vertebral Fracture in Women

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Abstract

Objective: To investigate the association between body mass index (BMI), waist circumference (WC), and vertebral fracture (VF) risk in women.

Methods: This prospective study was conducted in 54,934 Nurses' Health Study participants. BMI was assessed biennially and WC was assessed in 2000. Self-reports of VF were confirmed by record review. BMI reflects lean body mass and WC reflects abdominal adiposity when included in the same regression model.

Results: Our study included 536 VF cases (2002 to 2014). Compared with women with BMI 21.0-24.9kg/m^2, the multivariable-adjusted relative risk (MVRR) of VF for women with BMI≥32.0kg/m^2 was 0.84 (95%CI 0.61,1.14; p_{trend}=0.08). After further adjusting for WC, the MVRR of VF for women with BMI≥32.0kg/m^2 was 0.70 (95%CI 0.49,0.98; p_{trend}=0.003). Compared with women with WC<71.0cm, the MVRR of VF for women with WC≥108.0cm was 1.76 (95%CI 1.06,2.92; p_{trend}=0.01), and after further adjusting for BMI was 2.49 (95%CI 1.44,4.33; p_{trend}<0.001).

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Conclusions: Greater lean body mass was independently associated with lower VF risk. Larger WC was independently associated with higher VF risk. These findings suggest that fat distribution is an important predictor of VF, and that avoiding central adiposity, as well as maintaining muscle mass, may potentially confer reduced risk of VF in older women.

Keywords

Body Mass Index; Waist Circumference; Vertebral Fracture; Prospective Study; Nurses' Health Study

Introduction

Vertebral fracture (VF) represents the most common type of fracture and confers significant disability , morbidity and mortality (1). The incidence of VF increases with age (2), with up to twenty-five percent of postmenopausal women estimated to have sustained a VF in the United States (3). Because of differences in vertebral microarchitecture (4), compressive loading (5), and biomechanical stress (6), vertebral fracture risk factors may vary from those for other fracture locations.

Obesity has long been postulated to be protective against fractures (7) because it is associated with higher bone mineral density (BMD). However, emerging evidence is challenging this concept (8, 9). The distribution of body fat, particularly abdominal obesity, may affect bone differently (10) than peripheral subcutaneous fat and potentially affect fracture risk (11). Moreover, the relation between obesity and risk of fracture also appears to depend on the fracture location (9). In a meta-analysis of body mass index (BMI) and risk of fracture, after adjusting for BMD, BMI was protective for hip fracture, but associated with higher risk for fractures of the upper arm, distal forearm, and tibia and fibula (12). However, this meta-analysis did not examine the association between BMI and VF.

We recently carried out a meta-analysis on the association between BMI and risk of VF in men and women. Amongst these prospective studies, we found no statistically significant association in women (13). However, we found substantial heterogeneity among the studies in women (14, 15, 16, 17, 18, 19). These studies did not include a measure of central obesity, such as waist circumference. Thus far, no study has examined the independent association between waist circumference and risk of VF in women.

Therefore, we conducted a prospective study on the association between BMI, waist circumference, and risk of incident clinical VF over a 12-year period in 54,934 women in the Nurses' Health Study (NHS).

Methods

Study Population

The NHS is a prospective cohort study, enrolling 121,700 female nurses 30-55 years of age in 1976. Since then, biennial mailed questionnaires have been sent to participants with comprehensive questions on newly diagnosed diseases, medications, and lifestyle practices

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with >90% follow-up of the eligible person-time. The vast majority (97%) of the participants are white.

The current analysis includes 54,934 women who responded to the 2012 or 2014 questionnaire which asked about VF history, and who also had available information on BMI or waist circumference. Exclusion criteria for this analysis were prior history of fracture (hip or wrist) or cancer (other than non-melanoma skin cancer). Information on BMI was obtained throughout the follow-up period. The Brigham and Women's Hospital Institutional Review Board approved the study protocol.

Assessment of Body Mass Index and Waist Circumference

Weight has been queried on every biennial questionnaire in NHS. Among a subset of participants who directly measured their weight, self-reported weight was highly reliable (r=0.97) (20). BMI (kg/m^2) was calculated from the information provided by participants on weight and height. We ultimately categorized BMI in our models as <21.0 kg/m^2, 21.0-24.9 kg/m^2, 25.0-29.9 kg/m^2, 30.0-31.9 kg/m^2 and ≥32.0 kg/m^2.

Waist circumference was queried among NHS participants in 1986, 1996, and 2000. Among a subset of NHS participants who directly measured their waist circumference, self-reported waist circumference was highly reliable (r=0.88) (20). For participants who did not provide waist circumference information in 2000, we carried forward information provided on waist circumference in 1996 if available.

Assessment of Covariates

Potential confounders ascertained from the questionnaires included age, race (white or non-white), physical activity (quintiles of metabolic equivalent task scores), smoking status (never, past, current), history of self-reported falls, hypertension, diabetes, self-reported osteoporosis, and physical examination during the previous two years. Use of postmenopausal hormones, bisphosphonates, diuretics, and proton-pump inhibitors was also queried. Self-reported physical activity was validated previously when compared with physical activity diaries (r=0.79) in a similar cohort (21). Hypertension and diabetes history were previously validated in this cohort. Self-reported osteoporosis was validated recently in a similar cohort (22).

Semi-quantitative food-frequency questionnaires (FFQs) were used to assess dietary intake. These extensively validated (23) questionnaires inquired about the average intake during the previous year of >130 individual food items and >20 beverages, as well as supplements and vitamins. Food frequency questionnaires were mailed to participants in 2002, 2006, and 2010. The variables considered in our models were quintiles of dietary intakes of caffeine, protein, magnesium, phosphorus, vitamin A, vitamin D, calcium, alcohol intake (none, 0.1-4.9 g/day, 5-14.9 g/day, ≥ 15 g/day), supplemental vitamin D intake (none, 1-400 IU/day, >400 IU/day), and supplemental calcium intake (none, 1-500 mg/day, >500 mg/day).

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Ascertainment of Clinical Vertebral Fracture

Ascertainment of clinical vertebral fracture in NHS was previously described elsewhere (24, 25). The 2012 questionnaire asked participants about lifetime history of a clinician-diagnosed "vertebral (spine) fracture, x-ray confirmed" and the year of first diagnosis. The 2014 questionnaire asked participants again about a VF diagnosis. A supplemental questionnaire was mailed to participants who reported a VF in 2002 or afterwards. Permission was requested to obtain participants' medical records related to the VF. Among the participants who gave consent and for whom sufficient information was available in the medical records to make a diagnosis, we confirmed VF cases by radiology report (e.g., magnetic resonance imaging, computed tomography scan, or x-ray) or medical report (e.g., hospital discharge summary, operative note, clinic visit note, or operative note).

If the word "fracture" (e.g., "vertebral fracture", "wedge fracture", "compression fracture", "spine fracture") or language to suggest a VF (e.g., "vertebral collapse", "severe wedge compression", "acute compression") was contained in the radiology or medical report, then a self-reported VF was confirmed as a case. One of the authors (HNR), who was blinded to exposure status, adjudicated records containing less definitive language for a VF. When a VF diagnosis was less clear (e.g. "mild compression deformity"), participants were coded as "probable" cases and were excluded from our analysis.

Vertebral fractures associated with low or moderate level trauma (e.g. slipping, tripping) were included in our analysis. Vertebral fractures associated with motor vehicle accidents, horseback riding accidents, bicycle accidents, or high trauma were not included in our analysis. Cervical or sacral fractures were also excluded. Only confirmed cases of VF diagnosed between 2002 to May 31, 2014 were included in our analysis.

Statistical Analyses

The study design was prospective; information on BMI, waist circumference and the covariates of interest was gathered before the VF diagnosis. We counted person-time of follow-up from the date of return of the 2002 questionnaire to whichever of the following occurred first: 1) the date of VF diagnosis, 2) death, or 3) May 31, 2014. During the follow-up period, we censored participants if they developed a hip fracture or any cancer (other than non-melanoma skin cancer). Information on BMI and other covariates was collected from the baseline questionnaire. We used updated information from subsequent questionnaires to update the exposure status at the start of each follow-up period. Our analysis used period-specific categories of BMI and other covariates. The interpretation of BMI is altered when waist circumference and BMI are in the same multivariable model, and now reflects lean body mass (26). The interpretation of waist circumference reflects abdominal adiposity when waist circumference and BMI are included in the same multivariable model (26). Cox proportional-hazards models were used to adjust for potential confounders as listed above. All P values are two-tailed. The analysis was performed using SAS 9.4 (SAS Institute, Cary, NC).

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Results

Body Mass Index and Risk of Vertebral Fracture

Over 12 years with 597,295 person-years of follow-up, there were 536 confirmed VF cases. Table 1 shows the cohort characteristics in 2002 according to BMI. However, for our analyses, we used for each time period the updated information on BMI and covariates. In 2002, the median BMI was 26.0 kg/m^2. By 2012, the median BMI was 25.7 kg/m^2. The Spearman correlation coefficient for the association between waist circumference and BMI was 0.71 ($p<0.0001$) in 2002 and decreased to 0.62 ($p<0.0001$) by 2010. In 2002, women with higher BMI were slightly younger, less physically active, less likely to be taking a calcium supplement, had lower total vitamin D intake, higher protein intake, lower alcohol intake, and were more likely to have a history of falls, hypertension, and diabetes. They were less likely to report a history of osteoporosis or to be taking bisphosphonates. Almost all (99.3%) of the women were postmenopausal in 2002.

After adjusting for age, compared with women with BMI 21.0-24.9 kg/m^2, BMI ≥32 kg/m^2 was not significantly associated with risk of clinical VF (RR 0.84, 95%CI 0.63, 1.12; $p_{trend}=0.03$) (Table 2). After multivariable adjustment, compared with women with BMI 21.0-24.9 kg/m^2, the relative risk of clinical VF was 0.84 (95%CI 0.61, 1.14; $p_{trend}=0.08$) for women with BMI ≥32 kg/m^2. Following adjustment for waist circumference, the relative risk of clinical vertebral fracture was 0.70 (95%CI 0.49, 0.98; $p_{trend}=0.003$) for women with BMI ≥32 kg/m^2 compared with women with BMI 21.0-24.9 kg/m^2. The results were similar when we evaluated the association with baseline BMI (without updating of BMI) and BMI updated every two years.

Waist Circumference and Risk of Vertebral Fracture

Table 3 shows the cohort characteristics according to waist circumference in 2002. The median baseline waist circumference was 86.4 cm. In 2002, women with larger waist circumference were slightly younger, less physically active, less likely to be taking a calcium supplement, had lower total vitamin D intake, higher protein intake, lower alcohol intake, and were more likely to have a history of falls, hypertension, and diabetes. They were also less likely to report a history of osteoporosis or to be taking bisphosphonates.

After adjusting for age, compared with women with waist circumference <71.0 cm, women with waist circumference ≥108.0 cm had an increased risk of clinical VF (RR 1.72, 95%CI 1.05, 2.80; $p_{trend}=0.03$) (Table 4). Following multivariable adjustment, the relative risk was not appreciably altered (RR 1.76, 95%CI 1.06, 2.92; $p_{trend}=0.01$). After further adjustment for BMI, the relative risk of clinical VF was 2.49 (95%CI 1.44, 4.33; $p_{trend}<0.001$) for women with waist circumference ≥108.0 cm, compared with <71.0 cm.

Interaction Analyses

We examined whether the association between BMI and risk of VF varied by waist circumference, and whether the association between waist circumference and risk of VF varied by BMI. No statistically significant interaction was noted between waist circumference and BMI (p for interaction >0.87). We assessed whether the associations

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between measures of adiposity and vertebral fracture varied by bisphosphonate use, osteoporosis, or age (<=70 or >70 years). No statistically significant interaction was noted for BMI with bisphosphonate use (p for interaction >0.27), osteoporosis (p for interaction >0.25), or age (p for interaction >0.97). No statistically significant interaction was noted for waist circumference with bisphosphonate use (p for interaction >0.70), osteoporosis (p for interaction >0.33), or age (p for interaction >0.65).

A mediation analysis was also performed to quantify the proportion of the association between BMI, waist circumference and VF risk that could be explained by osteoporosis as an intermediate condition. History of osteoporosis explained 39.6% (95%CI 11.5%, 76.8%; p <0.0001) of the association between BMI and VF, and 33.2% (95%CI 1.3%, 94.8%; p <0.0001) of the association between waist circumference and VF.

Discussion

Our study of over 54,000 women found that larger waist circumference was independently associated with higher risk of clinical VF, while higher lean body mass was associated with lower risk. When waist circumference and BMI are in the same model, the interpretation of BMI is altered and reflects lean body mass to a greater degree, whereas waist circumference reflects abdominal adiposity. These findings suggest that the distribution of fat is an important predictor of vertebral fracture. There are a number of distinguishing strengths of our study, including the large number of incident clinical VF cases confirmed by record review, repeated assessment of BMI over time, and assessment of waist circumference.

The inverse association between lean body mass and VF risk was only evident after the addition of waist circumference to the multivariable model. In our recent meta-analysis on the association between BMI and VF, we did not find a statistically significant association between BMI and VF in women (RR = 0.98, 95%CI 0.8, 1.20, n=79,512 participants, n=1,296 vertebral fracture events) (13). However, none of the prior studies examining the association between BMI and VF risk included waist circumference in their models or studied the independent association between waist circumference and vertebral fracture risk.

There was also substantial heterogeneity across the previous studies in women (I^2=90.1%, p<0.001), which could have been due to adjustment for BMD, as well as methodological differences, including the definition of vertebral fracture as an outcome, paucity of vertebral fracture cases, measurement of obesity and body mass index, lack of inclusion or updating of important covariates during study follow-up, length of study follow-up, and choice of study population.

Moreover, BMI alone in a model may also be a less reliable marker of body fatness in older adults compared with younger populations (27). The components of BMI, fat mass and lean body mass vary by sex and age. For a given BMI, women have a higher percentage of body fat than men (28). BMI as a measure of adiposity has limitations in older adults. Changes in body composition with aging include loss of muscle mass and increase in fat mass (28). Moreover, fat distribution changes with aging. Therefore, collecting information on body fat distribution, such as waist circumference, a measure of central adiposity, can provide

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additional insights on body fat distribution in older adults (26). The current definition of metabolic syndrome for women includes a waist circumference > 88 cm. Our study underscores the importance of assessing BMI, as well as waist circumference when studying the association between adiposity and VF risk.

Emerging reports are challenging the concept that obesity is protective against all types of fractures. Different mechanisms have been suggested to elucidate the relation between fat mass, bone metabolism, and resulting fracture risk (29). As an active metabolic organ, adipose tissue can have important effects on bone quality, strength, and mass. Adipose tissue can also have hormonal effects on bone through increased adipokine production, e.g. adiponectin, a hormone linking bone and fat metabolism, as well as proinflammatory cytokines, all of which can inhibit bone formation and promote bone formation (29). Higher adipokine levels were associated with increased fracture risk in men (30, 31). The studies in women on the association between adipokine levels and fracture risk have reported less consistent findings (30, 31, 32). Lower insulin-like growth factor (IGF-1) levels may also disrupt bone homeostasis, thereby playing a role in mediating the harmful effects of visceral adiposity on bone health (33). The relation between obesity and VF risk may also be influenced by impaired biomechanical factors. Obesity, in particular abdominal obesity, could exert a negative effect on the bone's mechanical properties (34) as well as place an undue compressive load burden on the spine (35), thereby predisposing the vertebrae to fracture.

The location of fat tissue can also have exert differential effects on bone (e.g., subcutaneous versus visceral fat) (36). In a prior study conducted in NHS, abdominal adiposity was associated with increased hip fracture risk in women with low physical activity (11). Both visceral and total adiposity were associated with higher prevalent VF in women (37). Several prior studies reported an association between higher abdominal fat and lower BMD (33, 38).

In addition to the negative effects on bone as measured by BMD testing, visceral abdominal fat could detrimentally affect bone "quality" (e.g., bone microarchitecture, cortical porosity, bone matrix, mineralization, collagen deposition, geometry, and three-dimensional connectivity of bone) that is independent of bone mineral density. This negative effect of adipose tissue on bone quality may be more local or paracrine, rather than systemic (39). A study in healthy pre-menopausal women evaluated the association between trunk fat, as measured by dual-energy x-ray absorptiometry and helical quantitative computed tomography, and bone quality, as measured through transiliac crest bone biopsies, and reported that women in the highest tertile of trunk fat had inferior bone quality (10).

We also found that BMI, interpreted as greater lean body mass when in the same model with waist circumference, was independently associated with lower VF risk. Studies suggest that skeletal mass is positively associated with BMD (40) as well as trabecular bone geometry and microarchitecture (41). Aging is associated with loss of both lean muscle mass (sarcopenia) and muscle function (dynapenia) (42). Loss of trunk musculature can affect vertebral strength, as well as place undue compressive loading on vertebra (43). Therefore, sarcopenia (44) or sarcopenic obesity (45) could potentially be associated with higher fracture risk. However, further research is needed not only on the role of overall lean body

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mass, but specifically the role of trunk muscle strength and function and their association with risk of VF.

Our study has several limitations. There is the possibility of residual confounding given the observational study design. For example, we obtained information on self-reported history of osteoporosis, but did not have data available on morphometric fracture assessment or bone mineral density. Since our definition of clinical VF was based on review of medical records, we were unable to make a definitive VF diagnosis for some participants who self-reported a VF but did not provide permission or for whom we were unable to obtain their records. We recognize therefore, that our methods for ascertaining VF cases led to a lower observed incidence rate, but the associations should be valid as the ability to obtain records was not related to the exposures being studied. Our assessment of fat distribution was based on self-reported BMI and waist circumference, rather than body composition imaging studies. Given the observational study design, we cannot provide a definitive mechanism to explain our findings. Finally, our findings may not be necessarily generalizable to other races or men since our study population was almost entirely white and female. Future studies should consider examining whether a population at higher risk for metabolic syndrome (i.e., Asians, where there are lower waist circumference cut-offs than for Whites) is at higher risk for vertebral fracture at lower waist circumference values.

In conclusion, larger waist circumference, a measure of abdominal adiposity, was associated with higher risk of clinical VF in women. Moreover, higher lean body mass was associated with lower risk of clinical VF. These results suggest that avoiding central adiposity as well as maintaining muscle strength may potentially reduce the risk of VF in older women. Further research is warranted on body composition, particularly central adiposity, lean body mass, and vertebral fracture risk.

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Study Importance

- Vertebral fracture is the most common type of osteoporotic fracture. Previous studies on the relation between body mass index and vertebral fracture risk have been inconsistent and no prospective studies have investigated the relation between waist circumference and vertebral fracture risk.
- In this prospective study of over 54,000 women, we observed that larger waist circumference was independently associated with higher risk of clinical vertebral fracture, while greater lean body mass was independently associated with lower vertebral fracture risk.
- These findings suggest that fat distribution is an important predictor of vertebral fracture, and that avoiding central adiposity, as well as maintaining muscle mass, may potentially confer reduced risk of vertebral fracture in older women.

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Table 1

Age-Adjusted Baseline Characteristics of Participants in 2002 by Body Mass Index (kg/m^2)

	<21.0 (n=4,963)	**21.0 - 24.9 (n=17,589)**	**25.0 - 29.9 (n=19,487)**	**30.0 - 31.9 (n=4,591)**	**≥ 32.0 (n=8,304)**	**p-value**
Age, years [*]	67.0 (6.8)	66.3 (6.6)	66.0 (6.5)	65.6 (6.4)	64.4 (6.0)	< 0.001
Body Mass Index (kg/m^2)	19.8 (1.1)	23.2 (1.1)	27.3 (1.4)	30.9 (0.6)	36.2 (4.1)	<0.001
Waist Circumference (cm) [†]	72.7 (7.7)	80.0 (8.9)	89.2 (10.0)	97.0 (10.3)	104.5 (12.9)	<0.001
Physical Activity (METS/week) [†]	25.6 (27.1)	22.0 (23.3)	17.7 (20.5)	13.8 (20.2)	11.4 (18.7)	<0.001
Dietary Calcium (mg/day) [#]	861 (331)	860 (323)	855 (316)	847 (308)	846 (320)	<0.001
Calcium Supplement (mg/day)	715 (522)	680 (527)	605 (517)	563 (516)	510 (517)	<0.001
Calcium Supplement Use (yes/no), %	70.7	68.5	63.5	60.5	57.9	
Total Vitamin D Intake (IU/day) [#]	609 (353)	587 (338)	555 (329)	540 (329)	517 (321)	<0.001
Total Protein Intake (g/day) [#]	67.5 (12.9)	69.1 (12.7)	70.6 (12.9)	71.5 (13.2)	72.5 (13.4)	<0.001
Animal Protein Intake (g/day) [#]	42.8 (13.7)	45.0 (13.3)	47.0 (13.4)	48.2 (13.8)	49.4 (14.0)	<0.001
Total Vitamin A Intake (mcg/day) [#]	2,066 (1,539)	1,961 (1,410)	1,891 (1,347)	1,873 (1,358)	1,821 (1,277)	<0.001
Alcohol Intake (g/day)	8.1 (12.5)	7.7 (11.6)	5.9 (10.4)	4.5 (8.9)	3.2 (7.6)	<0.001
Smoking status						<0.001
Never smoker, %	48.5	46.5	46.4	48.0	47.4	
Past smoker, %	40.4	45.5	46.8	46.2	48.1	
Current smoker, %	11.1	8.0	6.8	5.8	4.5	
History of Falls, %	6.5	7.3	8.4	9.1	10.5	<0.001
History of Diabetes, %	2.7	3.7	7.6	11.9	19.5	<0.001
History of Hypertension, %	29.1	39.7	52.6	63.5	71.3	<0.001
Self-Reported Osteoporosis, %	23.2	16.7	12.2	9.7	8.3	<0.001
Postmenopausal Hormone Use, %	44.7	44.7	40.7	38.2	32.7	<0.001
Current Bisphosphonate Use, %	19.4	14.8	9.4	6.3	5.0	<0.001

[*] Value is not age adjusted

[†] Waist circumference, physical activity and history of falls were not asked about in 2002 so data are from the 2000 questionnaire.

#Energy adjusted.

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Table 2

Body Mass Index and Risk of Clinical Vertebral Fracture (2002-2014)

	Body Mass Index (kg/m^2)					
	<21.0	**21.0 - 24.9**	**25.0 - 29.9**	**30.0 - 31.9**	**≥ 32.0**	**P for trend**
Cases of Vertebral Fracture (n)	83	192	161	39	61	
Person-years	61,456	190,011	208,431	48,856	88,541	
Age-adjusted Relative Risk (95% CI)	1.15 (0.89, 1.48)	1.0	0.81 (0.66, 1.00)	0.88 (0.62, 1.24)	0.84 (0.63, 1.12)	0.03
Multivariate Relative Risk (95% CI) †	1.08 (0.84, 1.41)	1.0	0.84 (0.68, 1.04)	0.90 (0.63, 1.29)	0.84 (0.61, 1.14)	0.08
Multivariate Relative Risk + Waist Circumference (95% CI)	1.22 (0.93, 1.60)	1.0	0.77 (0.61, 0.96)	0.78 (0.54, 1.13)	0.70 (0.49, 0.98)	0.003

Body mass index was updated throughout the analysis period (2002-2014).

†The multivariate model includes race, physical activity, history of falls, smoking status, alcohol intake, supplemental calcium intake, quintiles of intake of dietary calcium, total vitamin D, vitamin A, and total protein, history of diabetes, hypertension, self-reported osteoporosis, postmenopausal hormone use, thiazide and furosemide use, proton pump inhibitor use, and recent physical exam.

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Table 3

Age-Adjusted Baseline Characteristics of Participants by Waist Circumference (cm)

	<71.0 (n=3,448)	71.0 - 79.9 (n=10,918)	80.0 - 88.9 (n=12,556)	89.0 - 98.9 (n=7,434)	99.0 - 107.9 (n=5,439)	≥108 (n=2,984)	p-value
Age, years *	64.8 (6.4)	65.5 (6.5)	66.5 (6.6)	67.0 (6.6)	67.2 (6.6)	66.3 (6.6)	<0.001
Body Mass Index (kg/m^2)	21.3 (2.6)	23.3 (2.7)	25.8 (3.3)	28.2 (3.9)	30.6 (4.5)	34.7 (5.9)	<0.001
Waist Circumference (cm) †	66.3 (2.8)	75.2 (2.8)	84.9 (2.8)	93.7 (2.1)	102.4 (2.8)	116.3 (7.9)	<0.001
Physical Activity (METS/week) †	27.4 (28.4)	23.7 (24.3)	19.2 (21.0)	16.6 (19.2)	13.8 (20.4)	11.2 (16.8)	<0.001
Dietary Calcium (mg/day) #	871 (339)	865 (321)	861 (321)	847 (309)	853 (315)	849 (324)	<0.001
Calcium Supplement (mg/day)	724 (529)	690 (523)	641 (519)	600 (520)	587 (519)	553 (534)	<0.001
Calcium Supplement Use (yes/no), %	70.8	68.8	66.4	63.2	61.5	59.2	
Total Vitamin D Intake (IU/day) #	607 (360)	590 (333)	575 (332)	554 (326)	554 (324)	540 (335)	<0.001
Total Protein Intake (g/day) #	68.6 (13.3)	69.1 (12.5)	69.7 (12.7)	70.4 (13.0)	70.9 (13.0)	72.4 (14.0)	<0.001
Animal Protein Intake (g/day) #	43.9 (14.2)	44.8 (13.2)	46.0 (13.3)	46.7 (13.5)	47.6 (13.5)	49.1 (14.5)	<0.001
Total Vitamin A Intake (mcg/day) #	2,090 (1,565)	2,006 (1,441)	1,935 (1,392)	1,884 (1,364)	1,895 (1,302)	1,896 (1,387)	<0.001
Alcohol Intake (g/day)	7.4 (10.9)	7.5 (11.5)	6.7 (10.8)	5.7 (10.3)	4.8 (9.9)	3.7 (8.9)	<0.001
Smoking status							<0.001
Never smoker, %	49.0	47.5	47.5	47.2	46.0	46.1	
Past smoker, %	41.8	45.3	45.5	46.8	48.4	49.1	
Current smoker, %	9.1	7.2	7.1	6.0	5.6	4.9	
History of Falls, %	6.4	7.2	8.2	8.4	9.8	11.1	<0.001
History of Diabetes, %	2.2	2.9	5.2	8.6	12.9	21.5	<0.001
History of Hypertension, %	29.9	37.6	47.7	56.4	63.6	70.6	<0.001
Self-Reported Osteoporosis, %	20.0	17.6	14.6	12.9	12.2	10.1	<0.001
Postmenopausal Hormone Use, %	45.9	46.3	42.6	41.4	38.4	34.6	<0.001
Current Bisphosphonate Use, %	16.8	16.1	12.5	9.2	8.9	6.6	<0.001

* Value is not age adjusted

† Waist circumference, physical activity and history of falls were not asked about in 2002 so data are from the 2000 questionnaire.

Energy adjusted.

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Table 4

Waist Circumference * and Risk of Clinical Vertebral Fracture

	Waist Circumference (cm)						
	<71.0	**71.0 - 79.9**	**80.0 - 88.9**	**89.0 - 98.9**	**99.0 - 107.9**	**≥108.0**	**P for trend**
Cases of Vertebral Fracture (n)	26	113	129	95	64	42	
Person-years	38,287	120,383	137,370	81,275	58,819	32,485	
Age-adjusted Relative Risk (95% CI)	1.0	1.32 (0.86, 2.02)	1.24 (0.81, 1.89)	1.47 (0.95, 2.28)	1.37 (0.87, 2.17)	1.72 (1.05, 2.80)	0.03
Multivariate Relative Risk (95% CI) †	1.0	1.33 (0.87, 2.04)	1.29 (0.85, 1.98)	1.58 (1.02, 2.46)	1.43 (0.90, 2.29)	1.76 (1.06, 2.92)	0.01
Multivariate Relative Risk + Body Mass Index (95% CI)	1.0	1.45 (0.94, 2.23)	1.55 (1.00, 2.42)	2.04 (1.28, 3.25)	1.93 (1.17, 3.19)	2.49 (1.44, 4.33)	<0.001

*Waist circumference was assessed in 2000. Waist circumference data from 1996 was used for participants who did not provide waist circumference data in 2000.

†The multivariate model includes race, physical activity, history of falls, smoking status, alcohol intake, supplemental calcium intake, quintiles of intake of dietary calcium, total vitamin D, vitamin A, and total protein, history of diabetes, hypertension, self-reported osteoporosis, postmenopausal hormone use, thiazide and furosemide use, proton pump inhibitor use, and recent physical exam.

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