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ORIGINAL ARTICLE

Abdominal obesity and hip fracture: results from the Nurses' Health Study and the Health Professionals Follow-up Study

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Abstract
Summary Abdominal obesity might increase fracture risk. We studied the prospective associations between waist circumference, waist-to-hip ratio, and hip fracture. The indicators of abdominal obesity were associated with increased hip fracture risk in women, but not in men. The increased risk was restricted to women with low physical activity.
Introduction Low weight is an established risk factor for osteoporosis and hip fracture. However, the association between fat tissue, muscle, and bone is complex, and abdominal obesity might increase fracture risk. We studied the prospective associations between indicators of abdominal obesity and hip fracture in two large US cohorts.
Methods At baseline in 1986 and through biennial follow-up, information on hip fracture and potential risk factors was collected in 61,677 postmenopausal women and 35,488 men above age 50. Waist and hip circumferences were reported at baseline and updated twice.
Results During follow-up, 1168 women and 483 men sustained a hip fracture. After controlling for known risk factors, there was a significant association in women between increasing waist circumference and hip fracture (RR per 10-cm increase 1.13 (95 % CI 1.04–1.23) and between increasing waist-to-hip ratio and hip fracture (RR per 0.1 unit increase 1.14 (95 % CI 1.04–1.23), but these associations were not seen in men. In women, both measures interacted with physical activity. Those in the highest (≥0.90) versus lowest (<0.75) category of waist-to-hip ratio had increased risk of hip fracture if their activity was less than the population median (RR = 1.61, 95 % CI 1.18–2.19) but not if their activity was higher (RR = 1.00, 95 % CI 0.72–1.40). A similar pattern was found for waist circumference.
Conclusion Indicators of abdominal obesity were associated with increased hip fracture risk after controlling for BMI in women. The increased risk was restricted to women with low physical activity. In men, no significant associations were found.

Keywords Aging · Bone-fat interactions · Hip fracture · Obesity · Physical activity · Prospective

Introduction

Low body mass index (BMI) is an established and strong risk factor for osteoporosis and hip fracture [1–4]. With higher BMI, the risk of hip fracture might be reduced due to the loading effect of higher weight, more muscle mass, the padding effect of soft tissue over the hip, and aromatase in adipose tissue affecting sex hormone concentration [5, 6]. Both hip fracture and obesity are common and linked to increased

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morbidity and mortality. In the NHANES study, it was reported that 49 % of the hip fractures occurred on those overweight or obese [4]. Due to increasing weight in the population, a higher proportion of future fractures is expected to occur in the overweight and obese. In addition, the association between fat tissue, muscle, and bone is complex, and the view that obesity is protective against osteoporotic fractures has been challenged [4, 6, 7]. The inverse association between BMI and fracture risk has been reported to be non-linear, with risk leveling off in the overweight and obese range of BMI [1, 4]. In a large Norwegian study, abdominal obesity was associated with increased risk of hip fracture after adjustment for BMI (which in itself had a protective role) [8]. An adverse effect of abdominal fat is biologically plausible as inflammation has an adverse effect on bone tissue [5] and it could influence the risk of falling [9]. We aimed to study the association between waist circumference, hip circumference, waist to hip ratio, and incident hip fractures in the Nurses' Health Study I and the Health Professionals Follow-up Study.

Materials and methods

The Nurses' Health Study (NHS) began in 1976 with 121,700 female nurses 30 to 55 years of age, and the Health Professionals Follow-up Study (HPFS) was formed 10 years later with 51,529 male health professionals 40 to 75 years of age. The NHS and HPFS data are available upon application for academic research. Participants provided a medical history and information on lifestyle and disease risk factors on the initial questionnaire and have updated this information and reported incident diagnoses on subsequent biennial questionnaires. Participants live throughout the USA. Deaths were ascertained from family members, the postal service, and the National Death Index [10, 11].

Baseline for both men and women was the 1986 questionnaire cycle when waist and hip circumferences were first reported. Circumferences were updated twice over follow-up through 2012. For this longitudinal investigation, participants entered the study population when postmenopausal (women) or at age 50 or older (men) and had provided the most recent circumference measures. In order to start with a healthy cohort, participants were excluded at entry if they had reported a prior hip fracture or diagnosis of osteoporosis, cancer, cardiovascular disease, or diabetes. Those of African American or Asian ancestry (3 % of each cohort) were also excluded because of differing fracture risks. The final study populations included 61,677 women and 35,488 men. Completion and return of the self-administered questionnaires constituted informed consent. This investigation was approved by the Institutional Review Board at Brigham and Women's Hospital in Boston, MA.

Hip fractures

On every biennial questionnaire, participants were asked to report all hip fractures with the date of occurrence and a description of the circumstances. Type of hip fracture (cervical or trochanteric) was not requested. As health professionals, cohort members are expected to be capable of reporting these events; in a validation study, all obtained medical records confirmed the diagnosis [12]. Over follow-up from 1986 to 2012, 1244 hip fractures were identified on questionnaires or death certificates in the NHS study population and 569 were identified in HPFS. After excluding fractures due to malignancy or major traumatic events (e.g., motor vehicle accidents, downhill skiing), we included 1168 and 483 as cases in the NHS and HPFS analyses, respectively. Over 90 % of these fractures occurred when slipping, tripping, and falling from the height of a chair or from a similar low trauma event. The mean age at hip fracture was 74.8 years in NHS (range 47–91) and 76.9 years in HPFS (range 51–96).

Waist and hip circumferences and other exposures

In the 1986 cycle, participants were asked to report their waist and hip circumferences to the nearest one-fourth inch. A tape measure was provided with instructions to measure waist at the navel and hip at the largest circumference between navel and thighs. Assessments were repeated in 1996 and 2000 in women and 1996 and 2008 in men. The longest follow-up time without updates of waist and hip circumferences was thus from 2000 to 2012 in women and from 1996 to 2008 in men. The ratio of waist divided by hip was calculated at the three time points. Current weight to the nearest pound and height to the nearest inch were reported on the initial questionnaires in both cohorts, and current weight was updated on every subsequent biennial questionnaire. Current BMI (kg/m^2) was calculated from current weight and initial height. In a validation study among 140 NHS women and 123 HPFS men, self-reported body measures were compared with those collected by technicians on two seasonal visits. Correlations in NHS and HPFS, respectively, were 0.91 and 0.98 for waist circumference, 0.87 and 0.85 for hip circumference, and 0.98 and 0.96 for body weight [13]. In additional analyses, we also calculated a new alternative indicator of abdominal obesity, the body shape index (waist circumference/ ($BMI^{2/3} \times height^{1/2}$) [14].

Discretionary physical activity was assessed on biennial questionnaires as the average time per week spent during the past year in 11 specified recreational and outdoor activities, and energy expenditure from these activities was calculated in metabolic-equivalent hours per week (MET-h/week). The activity questionnaire was validated in the women and men in comparison with 7-day diaries [15, 16]. Difficulties with climbing a flight of stairs or walking one block were included on questionnaires beginning in 1992 in NHS and 1988 in HPFS. In NHS, general health status was asked for in 1992, 1996, and 2000. In both cohorts, diet was assessed every 4 years with a validated food frequency questionnaire (FFQ) [17, 18] on which participants reported their frequency of consumption over the previous year for specified amounts of more than 130 foods and alcoholic beverages. Nutrient intakes were calculated from the reported food frequencies and use of multivitamins and nutrient supplements and were adjusted for total energy intake [19]. Other measures, including smoking status and number of cigarettes smoked per day and current use of postmenopausal hormones (women only), thiazide diuretics, furosemide-like diuretics (e.g., Lasix®, Bumex®), and oral steroids, were assessed on all biennial questionnaires.

Statistical analysis

Participants contributed person-time from the return date of the 1986 baseline questionnaire if they provided waist and hip measures and women were postmenopausal or men were age 50 or older. Otherwise, participants entered the study at a later questionnaire (1988–2008 in NHS; 1988–2004 in HPFS) once menopause or age 50 was reached and the most recent waist and hip measures were reported. Participants were followed up to the date of hip fracture, last questionnaire response, or the end of study on 1 June 2012 in NHS and 1 January 2012 in HPFS. The study population of 61,677 women contributed 898,929 person-years and the study population of 35,488 men contributed 568,994 person-years.

We used Cox proportional hazards models to compute hazard ratio, hereafter called relative risk (RR), of hip fracture with 95 % confidence intervals (CI) within pre-defined evenly spaced categories of the updated waist and hip circumferences and waist/hip ratio. Models were rerun with continuous exposure data to test for linearity (P_{linear}). All models were conditioned on months of age and questionnaire cycle to account for age and time. Baseline height and BMI that was updated when waist and hip were updated were added to the basic model, followed by the addition of physical activity that was cumulatively averaged over follow-up. Fully adjusted RRs were calculated from models with the addition of assessed risk factors for hip fracture using time-varying data; i.e., person-time was assigned to the appropriate category for each variable at the beginning of every biennial questionnaire cycle.

Table 1 Age and age-adjusted characteristics[a] of women in the Nurses' Health Study within categories of current waist circumference at the approximate mid-point of follow-up in 1996

Current waist circumference (cm)					
% Of population	<72 16 %	72–79 21 %	80–87 27 %	88–95 18 %	≥96 18 %
Age, years	62.3	63.1	64.0	64.7	64.6
Height, 1986, cm	162	164	164	164	165
BMI, current (kg/m^2)	21.3	23.2	25.4	27.7	31.6
Dietary intake					
Calcium[b], mg	1101	1092	1057	1051	1038
Vitamin D[b], μg	9.6	9.4	9.1	9.1	9.1
Retinol[b], μg	1290	1231	1221	1184	1207
Protein[b], g	73.0	73.8	74.5	75.3	76.1
Vitamin K[b], mg	192	183	180	176	173
Caffeine, mg	273	270	268	261	259
Alcohol, g	6.2	6.2	5.9	5.6	4.5
Activity[c], MET-h/week	22.7	19.9	17.6	15.5	13.1
Difficulty climbing stairs or walking one block, %	3	3	4	5	9
General health status, not excellent (%)	9	9	11	13	18
Current smoker, %	17	13	12	11	9
Medication use					
Current HRT use, %	52	52	47	45	40
Thiazide diuretic, %	5	6	8	11	14
Furosemide diuretic, %	1	1	2	2	4
Oral steroids, %	2	2	2	2	3

[a] Values are means and percentages and were standardized to the age distribution of the study population in 1996

[b] Intake from foods and supplements adjusted for total energy intake

[c] Metabolic equivalent hours per week from discretionary physical activity (e.g., 12 MET-h/week is equivalent to 4 h/week of walking or 1 h/week of running)

Participants did not contribute person-time in cycles in which they were missing waist or hip circumference or BMI. Multiplicative interactions between exposures were calculated using the Wald test for continuous data ($P_{\text{interaction}}$). Specifically, we examined whether the associations between waist and hip circumferences and waist/hip ratio and risk of hip fracture differed by age, physical activity, BMI, or current use of postmenopausal hormones. Statistical significance was determined by $p<0.05$. The proportional hazard assumption was tested by the interaction terms between age and waist circumference, hip circumference, and waist-to-hip ratio, respectively.

Results

Age-adjusted characteristics at the approximate mid-point of follow-up in 1996 within categories of current waist circumference are shown for women in Table 1 and for men in Table 2.

On average, women and men with higher waist circumference were taller, had a higher BMI, were less engaged in physical activity and were more likely to have difficulties climbing a flight of stairs or walking a block, and were more likely to use a diuretic. Dietary intakes did not differ substantially by waist circumference. Whereas smoking was inversely associated with waist circumference in women, there was no clear trend in men. However, the smoking prevalence was low in men.

Current waist circumference was correlated with current BMI ($r=0.75$, $p<0.001$ in women and $r=0.78$, $p<0.001$ in men). The correlation between current hip circumference and current BMI was even higher in women ($r=0.84$, $p<0.001$), but not in men ($r=0.72$, $p<0.001$), whereas the correlation between current waist-to-hip ratio and current BMI was substantially weaker in both women ($r=0.29$, $p<0.001$) and men ($r=0.30$, $p<0.001$). The correlation between body height and BMI was $r=-0.06$ in women and $r=-0.006$ in men.

In NHS, median follow-up time was 14.2 years (range 0.2–26.0 years) in all women and 12.6 years (range 0.2–25.9 years) in women who sustained a hip fracture. The corresponding figures in HPFS were 15.9 years (range 0.1–26.0 years) in all men and 13.3 years (range 0.1–25.3 years) in men who sustained a hip fracture.

In analyses adjusted for age and cycle only, there was an inverse association between waist circumference and the risk of hip fracture in women (Table 3). The same was the case for hip circumference, whereas a weak positive association

Table 2 Age and age-adjusted characteristics[a] of men ages 50 and older in the Health Professionals Follow-up within categories of current waist circumference at the approximate mid-point of follow-up in 1996

Current waist circumference (cm)					
% Of population	<89 19 %	89–94 22 %	95–100 24 %	101–106 19 %	≥107 16 %
Age, years	64.3	65.6	66.6	67.1	67.5
Height, 1986, cm	176	178	179	180	181
BMI, current (kg/m^2)	22.8	24.1	25.7	27.2	30.4
Daily intakes					
Calcium[b], mg	938	911	900	893	913
Vitamin D[b], µg	11.2	10.8	10.5	10.2	10.4
Retinol[b], µg	1565	1466	1448	1413	1453
Protein[b], g	89.0	89.1	89.5	90.3	92.1
Vitamin K[b], mg	188	180	178	179	179
Caffeine, mg	202	216	227	245	256
Alcohol, g	10.4	11.0	11.5	11.8	11.5
Activity[c], MET-h/week	35.0	30.2	27.6	24.4	21.1
Difficulty climbing stairs or walking one block, %	2	2	2	6	5
Current smoker, %	6	5	5	6	5
Medication use					
Thiazide diuretic, %	2	4	4	5	7
Furosemide diuretic, %	1	1	1	2	3
Oral steroids, %	1	1	1	1	1

[a] Values are means and percentages and were standardized to the age distribution of the study population in 1996

[b] Intake from foods and supplements adjusted for total energy intake

[c] Metabolic equivalent hours per week from discretionary physical activity (e.g., 12 MET-h/week is equivalent to 4 h/week of walking or 1 h/week of running)

Table 3 Risk of hip fracture according to waist circumference, hip circumference, and waist-to hip ratio among women, the Nurses' Health Study (1986–2012)

Crude

	Cases	Person-years	Incidence/10,000[a]	RR (95 % CI) (age and cycle adjusted)	RR (95 % CI) (+ BMI and height)	RR (95 % CI) (+ physical activity)	RR (95 % CI) (fully adjusted[b])
Waist circumference (cm)							
<72	198	171,912	11.5	1.00	1.00	1.00	1.00
72–	243	211,247	11.5	0.84 (0.69–1.01)	0.92 (0.76–1.12)	0.90 (0.74–1.09)	0.93 (0.76–1.13)
80–	323	239,476	13.5	0.84 (0.70–1.00)	1.08 (0.88–1.32)	1.02 (0.83–1.25)	1.04 (0.84–1.28)
88–	211	142,081	14.9	0.80 (0.66–0.98)	1.24 (0.97–1.58)	1.13 (0.89–1.45)	1.15 (0.90–1.46)
≥96	193	134,209	14.4	0.76 (0.62–0.93)	1.54 (1.15–2.05)	1.34 (1.00–1.80)	1.33 (0.99–1.79)
P_{trend}				0.018	<0.0001	0.0016	0.003
RR per 10-cm increase				0.94 (0.90–0.99)	1.19 (1.10–1.28)	1.14 (1.05–1.23)	1.13 (1.04–1.23)
Hip circumference (cm)							
<95	312	210,603	14.8	1.00	1.00	1.00	1.00
95–	269	204,948	13.1	0.87 (0.74–1.03)	0.91 (0.76–1.08)	0.90 (0.75–1.07)	0.94 (0.78–1.12)
100–	236	176,976	13.3	0.83 (0.70–0.99)	0.93 (0.75–1.14)	0.89 (0.73–1.10)	0.95 (0.78–1.17)
105–	165	130,707	12.6	0.80 (0.66–0.97)	0.97 (0.76–1.24)	0.93 (0.72–1.19)	0.99 (0.77–1.28)
≥110	186	175,691	10.6	0.65 (0.54–0.78)	0.98 (0.72–1.33)	0.90 (0.66–1.23)	0.94 (0.69–1.29)
P_{trend}				<0.0001	0.60	0.26	0.53
RR per 10-cm increase				0.85 (0.80–0.91)	0.97 (0.85–1.10)	0.93 (0.82–1.06)	0.96 (0.85–1.09)
Waist-to-hip ratio							
<0.75	155	178,982	8.7	1.00	1.00	1.00	1.00
0.75–	236	228,882	10.3	0.98 (0.80–1.21)	1.06 (0.86–1.31)	1.04 (0.85–1.28)	1.04 (0.84–1.28)
0.80–	284	206,253	13.8	1.13 (0.92–1.38)	1.30 (1.06–1.59)	1.26 (1.03–1.55)	1.24 (1.01–1.52)
0.85–	232	143,436	16.2	1.13 (0.92–1.40)	1.40 (1.12–1.73)	1.33 (1.07–1.65)	1.29 (1.04–1.61)
≥0.90	261	141,372	18.5	1.10 (0.89–1.36)	1.43 (1.15–1.78)	1.34 (1.08–1.67)	1.29 (1.04–1.61)
P_{trend}				0.11	<0.0001	0.0004	0.0016
RR per 0.1 unit increase				1.06 (0.99–1.15)	1.19 (1.10–1.29)	1.16 (1.07–1.25)	1.14 (1.05–1.23)

[a] Crude incidence per 10,000 person-years

[b] Adjusted for age, questionnaire cycle, BMI (continuous, updated when waist and hip circumference were updated), height, physical activity, postmenopausal hormones, smoking status, use of furosemide diuretics, thiazide diuretics, and oral steroids, and intakes of calcium, vitamin D, retinol, protein, caffeine, and alcohol

between waist-to-hip ratio and hip fracture risk was suggested. After controlling for BMI and height, there was a clear positive association between waist circumference and hip fracture risk and between waist-to-hip ratio and hip fracture risk, which was somewhat attenuated after adjustment for physical activity. In the fully adjusted model, there were still significant positive associations between waist circumference, waist-to-hip ratio, and subsequent hip fracture. There was also a positive association between body shape index and the risk of hip fracture in women (RR 1.11 (1.04–1.18) per 1 SD increase (0.073 units) in the fully adjusted model). The corresponding RR for 1 SD increase (12.75 cm) in waist circumference was 1.17 (1.06–1.30) and for 1 SD increase (0.083 units) in waist-to-hip ratio 1.12 (1.04–1.19). On the other hand, there was no significant association between hip circumference and hip fracture after controlling for BMI, indicating that the association between waist-to-hip ratio and fracture risk was driven by the waist component.

Difficulties climbing a flight of stairs or walking a block and general health status were only asked for in some of the cycles, and additional analyses restricted to these cycles showed that adjustment for these variables did not affect the estimates substantially (data not shown). Neither did the estimates change much when adjusting for incident diabetes mellitus, cardiovascular diseases, or cancer (data not shown).

In women, the interaction terms between waist circumference and physical activity ($p = 0.03$) and between waist-to-hip ratio and physical activity ($p = 0.001$) were significant, and results stratified on physical activity are shown in Table 5. In women with little physical activity (less than the median (13.6 MET-h/week)), being in the highest category of waist circumference (≥96 cm) conferred a 58 % increased risk of hip

Table 4 Risk of hip fracture according to waist circumference, hip circumference, and waist-to hip ratio among men, the Health Professionals Follow-up Study (1987–2012)

Crude							
	Cases	Person-years	Incidence/10,000[a]	RR (95 % CI) (age and cycle adjusted)	RR (95 % CI) (+ BMI and height)	RR (95 % CI) (+ physical activity)	RR (95 % CI) (fully adjusted[b])
Waist circumference (cm)							
<89	93	116,689	8.0	1.00	1.00	1.00	1.00
89–	104	134,247	7.7	0.83 (0.62–1.10)	0.89 (0.65–1.21)	0.86 (0.63–1.18)	0.85 (0.62–1.16)
95–	117	134,200	8.7	0.86 (0.65–1.14)	0.99 (0.71–1.38)	0.95 (0.68–1.33)	0.94 (0.67–1.30)
101–	94	98,867	9.5	0.89 (0.66–1.20)	1.06 (0.72–1.56)	0.98 (0.66–1.44)	0.95 (0.64–1.40)
≥107	75	84,294	8.9	0.80 (0.59–1.10)	0.90 (0.56–1.46)	0.81 (0.50–1.31)	0.78 (0.48–1.27)
P_{trend}				0.59	0.61	0.96	0.79
RR per 10-cm increase				0.97 (0.88–1.07)	1.04 (0.89–1.22)	1.00 (0.85–1.17)	0.98 (0.83–1.15)
Hip circumference (cm)							
<95	86	85,130	10.1	1.00	1.00	1.00	1.00
95–	113	148,795	7.6	0.79 (0.59–1.05)	0.81 (0.59–1.11)	0.80 (0.59–1.10)	0.82 (0.60–1.12)
100–	132	156,219	8.5	0.85 (0.64–1.12)	0.92 (0.66–1.29)	0.90 (0.64–1.25)	0.91 (0.65–1.27)
105–	65	95,624	6.8	0.71 (0.51–0.98)	0.83 (0.55–1.25)	0.79 (0.52–1.19)	0.78 (0.52–1.19)
≥110	87	82,529	10.5	1.04 (0.76–1.42)	1.27 (0.80–2.01)	1.17 (0.74–1.86)	1.15 (0.72–1.82)
P_{trend}				0.92	0.71	0.99	0.87
RR per 10-cm increase				1.00 (0.89–1.12)	1.04 (0.87–1.23)	1.00 (0.84–1.19)	0.99 (0.83–1.18)
Waist-to-hip ratio							
<0.91	99	139,337	7.1	1.00	1.00	1.00	1.00
0.91–	86	113,071	7.6	0.96 (0.71–1.29)	1.00 (0.74–1.35)	1.00 (0.74–1.34)	0.99 (0.74–1.34)
0.94–	91	115,395	7.9	0.85 (0.64–1.14)	0.91 (0.68–1.22)	0.90 (0.67–1.21)	0.89 (0.66–1.19)
0.97–	81	78,743	10.3	1.01 (0.75–1.37)	1.13 (0.83–1.53)	1.10 (0.81–1.50)	1.09 (0.80–1.49)
≥1.00	126	121,752	10.3	0.94 (0.72–1.24)	1.09 (0.81–1.45)	1.05 (0.79–1.40)	1.04 (0.78–1.38)
P_{trend}				0.56	0.70	0.87	0.96
RR per 0.1 unit increase				0.96 (0.82–1.12)	1.03 (0.88–1.21)	1.01 (0.86–1.19)	1.00 (0.86–1.18)

[a] Crude incidence per 10 000 person-years

[b] Adjusted for age, questionnaire cycle, BMI (categorical), height, physical activity, smoking status, use of furosemide diuretics, thiazide diuretics, and oral steroids, and intakes of calcium, vitamin D, retinol, protein, caffeine, and alcohol

fracture compared to the lowest category (<72 cm) in the fully adjusted model. A similar pattern was found for waist-to-hip ratio with a 61 % increased risk in the highest category of waist-to-hip ratio. In contrast, there was no significant association between waist circumference or waist-to-hip ratio and hip fracture in women with physical activity above the median.

In women, the interaction terms between waist circumference and BMI and waist-to-hip ratio and BMI did not reach statistical significance ($p = 0.062$ and $p = 0.25$ respectively), and neither did waist circumference nor waist-to-hip ratio interact with age or current use of postmenopausal hormones.

In men, we found no significant associations between waist circumference, hip circumference, waist-to-hip ratio, and hip fracture (Table 4). The interaction term between waist-to-hip ratio and physical activity reached statistical significance ($p = 0.038$), but analyses stratified on physical activity did not show any significant associations (RR per 0.1 unit increase in waist-to-hip ratio = 1.18 (0.93–1.48) in men with physical activity less than the median (22.9 MET-h/week) and RR per 0.1 unit increase = 0.81 (0.63–1.05) in men with physical activity above the median). There were no significant interactions with waist circumference, age, or BMI.

In additional analyses, in which persons with osteoporosis, cancer, cardiovascular disease, or diabetes at baseline were not excluded, the associations between abdominal obesity and hip fracture changed little as compared to Tables 3 and 4 (RR per 10-cm increase in waist circumference = 1.14 (95 % CI 1.07–1.23) in women and 0.99 (95 % CI 0.86–1.14) in men; RR per 0.1 unit increase in waist-to-hip ratio = 1.14 (95 % CI 1.07–1.23) in women and 0.96 (95 % CI 0.84–1.11) in men).

Table 5 Risk of hip fracture according to waist circumference and waist-to hip ratio by strata of physical activity among women, the Nurses' Health Study (1986–2012)

	Cases	Person-years	Crude incidence/ 10,000[a]	RR (95 % CI) (age and cycle adjusted)	RR (95 % CI) (fully adjusted[b])
Physical activity < median[c]					
Waist circumference (cm)					
<72	84	70,521	11.9	1.00	1.00
72–79	123	95,272	12.9	0.88 (0.66–1.16)	1.02 (0.76–1.37)
80–87	182	119,771	15.2	0.86 (0.66–1.12)	1.18 (0.88–1.58)
88–95	135	79,263	17.0	0.82 (0.62–1.09)	1.34 (0.96–1.88)
≥96	139	84,380	16.5	0.76 (0.57–1.01)	1.58 (1.06–2.35)
RR per 10-cm increase				0.93 (0.87–0.99)	1.13 (1.02–1.26)
Waist-to-hip ratio					
<0.75	66	79,015	8.4	1.00	1.00
0.75–	130	109,245	11.9	1.15 (0.85–1.55)	1.27 (0.93–1.72)
0.80–	157	105,276	14.9	1.29 (0.96–1.73)	1.49 (1.10–2.01)
0.85–	134	75,877	17.7	1.26 (0.93–1.71)	1.53 (1.12–2.10)
≥0.90	176	79,795	22.1	1.30 (0.96–1.75)	1.61 (1.18–2.19)
RR per 0.1 unit increase				1.10 (0.99–1.21)	1.19 (1.07–1.32)
Physical activity ≥ median[c]					
Waist circumference (cm)					
<72	114	101,078	11.3	1.00	1.00
72–79	120	115,725	10.4	0.76 (0.58–0.99)	0.84 (0.63–1.11)
80–87	141	119,567	11.8	0.75 (0.58–0.97)	0.94 (0.69–1.26)
88–95	76	62,771	12.1	0.64 (0.47–0.87)	0.94 (0.64–1.37)
≥96	54	49,798	10.8	0.59 (0.42–0.83)	1.07 (0.67–1.71)
RR per 10-cm increase				0.89 (0.82–0.97)	1.10 (0.97–1.26)
Waist-to-hip ratio					
<0.75	89	99,711	8.9	1.00	1.00
0.75–	106	119,440	8.9	0.82 (0.61–1.09)	0.90 (0.67–1.20)
0.80–	127	100,800	12.6	0.94 (0.71–1.25)	1.07 (0.80–1.43)
0.85–	98	67,471	14.5	0.96 (0.71–1.30)	1.15 (0.84–1.57)
≥0.90	85	61,516	13.8	0.77 (0.56–1.06)	1.00 (0.72–1.40)
RR per 0.1 unit increase				0.95 (0.85–1.07)	1.06 (0.93–1.20)

[a] Per 10 000 person-years

[b] Adjusted for age, questionnaire cycle, BMI (continuous, updated when waist and hip circumference were updated), height, physical activity, postmenopausal hormones, smoking status, use of furosemide diuretics, thiazide diuretics, and oral steroids, and intakes of calcium, vitamin D, retinol, protein, caffeine, and alcohol

[c] Median physical activity was 13.6 MET-h/week

Discussion

In women, indicators of abdominal obesity were associated with increased risk of hip fracture after controlling for BMI. Interestingly, the increased risk was restricted to women with low physical activity. In men, no significant associations were found. After controlling for BMI, we found no clear association between hip circumference and hip fracture, neither in women nor in men.

Comparison with other studies

Our findings in women are in accordance with a large Norwegian cohort study reporting that high waist circumference and high waist-to-hip ratio were associated with increased risk of hip fracture in women (1498 hip fractures) after adjustment for BMI. However, in contrast to the present study, a similar increased risk was also found in Norwegian men (889 hip fractures) [8]. Also, in the Iowa Women's Health Study, the risk of hip fracture was positively associated with increasing waist circumference and waist-to-hip ratio in women after controlling for BMI [20, 21]. In the European EPIC cohort, no association between waist-to-hip ratio and hip fracture was found, but this study was limited to 203 hip fracture end points in women and 58 in men [22].

A high hip circumference is expected to reflect more soft tissue padding of the hip. However, as in the Norwegian study [8], we did not find an association between hip circumference and hip fracture after adjustment for BMI, which also is in agreement with the findings from the Iowa Women's Health Study [20, 21]. That said, the correlation between BMI and hip circumference was high, and the association between hip circumference and hip fracture might be captured by BMI. It could also be added that a protective effect of padding could be counteracted by a higher impact during a fall.

Possible mechanisms/explanations

Bone mineral density (BMD) is positively associated with increasing BMI, and previous studies have consistently reported an increased risk of hip fracture in lean women and men [1–3]. This might be due to several factors, including less mechanical loading on the skeleton, less muscle mass, less soft tissue padding over the hip, and less aromatase activity in soft tissue affecting sex hormone concentrations [5].

Both lean and fat mass contribute to body weight. A positive relation between total body fat mass and BMD has been reported [2, 5, 6, 23]. However, stratified on BMI or body weight, total body fat has been reported to be inversely associated with BMD [6]. Low-grade inflammation associated with obesity might be counterbalanced by positive factors associated with obesity such as more mechanical loading and estrogen [5]. However, even if a higher body weight overall might be beneficial for bone mass, fat distribution could modify this. Abdominal fat may influence bone independently of the effect of loading caused by high weight/BMI. Abdominal obesity might be related to increased hip fracture risk due to abdominal obesity-related inflammation [5, 24]. For example, inflammation might stimulate bone resorption and suppress bone formation due to inflammatory cytokines released by visceral adipocytes [25]. Inflammation might also influence negatively on bone microarchitecture [26], and an inverse association between abdominal fat and trabecular bone score, a bone quality index, has been reported [27]. Also, it has been postulated that abdominal obesity might increase the risk of falling due to instability and impaired balance [9]. Although nutritional factors could both be associated with abdominal obesity and influence the risk of fracture, adjustment for several nutritional risk factors (calcium, vitamin D, retinol, protein, caffeine, and alcohol) did not affect the associations between abdominal obesity and the risk of hip fracture substantially.

Interaction with physical activity

As previously reported, physical activity was associated with substantial reduced risk of hip fracture in women participating in the NHS [28]. A novel finding in the present analysis is the interaction between physical activity and abdominal obesity, as the increased risk of hip fracture only was seen in women with little physical activity. One possible explanation for this finding is that physical activity might offset the adverse metabolic consequences of abdominal obesity [29] or influence the risk of falling, which could be linked to weak muscles of the lower limbs.

Physical activity might also counteract fat infiltration of muscles/intermuscular adipose tissue (IMAT) [30] which has been related both to increased BMI and increased hip fracture risk [31].

It is also interesting to note that in bone marrow, adipocytes and osteoblasts originate from the same precursors, and physical activity might inhibit bone marrow adipose tissue differentiation and promote osteoblast differentiation [32].

Gender difference

The causes for the different findings in women and men are not clear. Men have more muscle and more bone than women, and there are some indications that the relation between fat and bone might differ across gender [6]. There could also be differences between the two cohorts that influence the results. The men in HPFS were dentists, veterinarians, pharmacists, etc., and the smoking prevalence was lower than in the nurses. It is also interesting to note that the men reported considerably higher levels of physical activity than the women. On the other hand, increasing waist circumference has previously been linked to increased risk of coronary heart disease in both cohorts [33]. Another possibility is that the gender difference could be due to chance. With substantially more hip fracture end points, the statistical power was higher in women than in men and the 95 % confidence intervals for the findings in women and men were overlapping.

Strength and weaknesses of the study

A strength of this study was the prospective design of two large cohorts with repeated assessments of waist and hip circumference and relevant other variables. A limitation is the self-report of fractures and the anthropometric measures. Also, results from this study may only be applicable to other Caucasian populations. In addition, it could be argued that health professionals are not representative of the general population. On the other hand, if a true effect of abdominal obesity on hip fracture risk exists, it would be expected to apply across occupational groups. Abdominal obesity could be an indicator of other factors influencing fracture risk. Although we have adjusted for a large number of potential confounders, residual confounding cannot be excluded. It is also a limitation that we did not have access to data on bone density, bone structure, and tissue thickness. Neither did we have information on history of falls, muscle mass, or strength. We can therefore not assess potential mechanisms for the association between abdominal obesity and the risk of hip fracture. It is easy to measure waist and hip circumference in clinical practice. However, further studies are warranted in order to elucidate if abdominal obesity influences on bone density and history of falls or acts by other means and thus gives added information.

It has been a concern that when assessing highly correlated variables like waist circumference and BMI, co-linearity might explain the association [2]. However, the correlation was much weaker between waist-to-hip ratio and BMI, and the findings were very similar for waist circumference and waist-to-hip ratio. In addition, the body shape index, constructed to be independent of both body weight and height and BMI [14], was also positively related to the risk of hip fracture. We did not adjust for previous fracture of any type, but analyses including or excluding persons with previous hip fracture when entering the study gave similar results. Baseline height was used to calculate BMI. In the previous Norwegian study [8], sensitivity analyses were performed to see if changes in BMI due to height loss influenced the associations between indicators of abdominal obesity and hip fracture. Adjustment for a recalculated BMI using previous body height collected on average 29 years before the baseline examination did not substantially influence on the results.

Conclusion

In summary, we found that among women, indicators of abdominal obesity were associated with increased risk of hip fracture after controlling for BMI. As the increased risk was restricted to women with low physical activity, physical activity could potentially counteract the increased risk associated with abdominal obesity. In men, no significant associations were found.

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Compliance with ethical standards

Conflicts of interest None.

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