Anthropometry, physical activity and hip fractures in the elderly

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Hip fractures constitute a major and growing public health problem amongst the elderly worldwide.[5,6,33,37] In 1990, approximately 1.66 million hip fractures occurred around the world, half of which were in Europe and North America, whereas, according to epidemiologic projections, this number is expected to increase to 6.26 million by the year 2050.[5,29] Amongst all bone fractures, hip fractures are the most devastating, because they are associated with considerable disability and loss of independence, diminished quality of life and reduced survival.[2,29,45] Furthermore, hip fractures impose substantial economic burden upon health-care services and upon society as a whole.[25]

The pathogenesis of bone fractures, and hip fracture in particular, is complex.[6,38] Impaired bone strength (a parameter depending on density, dimension and quality of the bone) and

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trauma from falling are the main conditions that, usually in combination, result in bone fracture amongst the elderly. Many factors seem to affect bone fracture risk by operating through these two underlying mechanisms (compromised bone strength and increased trauma occurrence) including underlying concurrent nosology, anthropometric characteristics and physical activity.[1,26,30]

Body mass index (BMI) below the normal has been reported to be associated with increased hip fracture risk amongst the elderly[27,28] over and beyond the risk attributed to the age-related decrease in bone mineral density.[8] There is also evidence that an increase in BMI (or body weight) is associated with lower hip fracture risk.[39,46] However, there seems to be no complete agreement with respect to the relationship of fat mass and adiposity with osteoporosis and age-related fractures.[43,53] Abdominal obesity, one of the components of metabolic syndrome, has been reported to increase hip fracture risk[13,51] and has been related both with higher[31,49] and lower[20,51] bone mineral density.

High stature is considered a risk factor for hip fracture[7,11,15,18] and mechanisms such as differences in the femoral geometry have been proposed to explain this association.[12,41]

Based on the current evidence from observational studies, moderate physical activity appears to reduce the risk of hip fractures in the elderly.[40] Physical activity can influence the risk of falling and a U-shaped association has been described between falls and physical activity intensity (the most active and most inactive individuals being at apparently higher risk).[3]

We have examined the relationship of anthropometry and physical activity with hip fracture incidence in a cohort of elderly Europeans from five countries, who were volunteers in the European Prospective Investigation into Cancer and nutrition (EPIC) study.

Materials and methods

Recruitment

EPIC is a multicentre, prospective cohort study aiming to investigate the role of biological, dietary, lifestyle and environmental factors in the aetiology of cancer and other chronic diseases. Study population selection criteria and data collection methodology for the EPIC study have been reported in detail elsewhere.[44] In brief, approximately 520 000 people enrolled between 1992 and 2000 in 23 research centres from 10 European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden and the United Kingdom). Participants were mainly between 35 and 70 years of age at enrolment and were recruited from the general adult population residing in a given town or geographical area with some exceptions: the French cohort was based on female members of the health insurance for teachers, the Utrecht cohort in the Netherlands recruited women attending breast-cancer screening, the Ragusa cohort in Italy was based on blood donors and their spouses, the Spanish cohorts was based on general population, blood donors and civil servants and the Oxford cohort in the UK recruited mostly vegetarian and health-conscious volunteers. The study protocol has been approved by ethics committees at the individual participating centres, whereas all participants signed informed consent forms before enrolment. All procedures have been in accordance with the Helsinki declaration for human rights.

Data from 30 274 elderly participants from seven centres in five European countries participating in the EPIC-Elderly Network on Ageing and Health (EPIC-Elderly-NAH) project were included in this analysis (for Italy, Varese and Ragusa; for Netherlands, Utrecht; for Greece, Athens; for Germany, Heidelberg and Potsdam; and for Sweden, Umea). The EPIC-Elderly-NAH project aims to investigate aspects of ageing of elderly Europeans and identify non-genetic predictors, with the use of baseline and follow-up data on risk factors, morbidity and cause-specific mortality. The source population of EPIC-Elderly-NAH is a cohort consisting of EPIC participants, who at recruitment were 60 years and older.[50] Amongst the EPIC centres, United Kingdom, Norway and the Italian centres of Turin, Florence and Naples did not participate in the EPIC-Elderly-NAH project, whereas three more countries could not be included in this analysis (in France, the site of the fracture was not recorded and centres in Spain and Denmark did not collect information on incident hip fractures).

Data collection

At baseline, a pre-coded questionnaire was used to record data on a number of lifestyle and health variables which, amongst others, included educational achievement, medical and reproductive history, smoking habits and physical activity.

The core physical activity questionnaire, either self- or interview-administered, focusses on three different types of physical activity: occupational, recreational and household.[16] An assessment of the reproducibility and relative validity of the non-occupational physical activity questions was undertaken in a sample of EPIC participants from the Netherlands. The Spearman correlation coefficients for the estimated reproducibility of the questionnaire over a 13-month period ranged from 0.47 to 0.89 in men, and from 0.49 to 0.81 in women, and for relative validity, as assessed by 3-day activity diaries, ranged from 0.32 to 0.81 for men, and from 0.28 to 0.72 for women. The questionnaire was found satisfactory for the ranking of subjects.[42] In Umea, Sweden, questions used for the assessment of physical activity were different from those in the EPIC core physical activity questionnaire, and subjects from this centre were not included in the present physical activity analysis. A summary leisure-time physical activity variable was created by combining recreational and household physical activities and was estimated by multiplying the time spent on each of a number of activities (walking, cycling, housework, gardening, do-it-yourself, sport and stair climbing), in hours per week, by an energy cost coefficient to convert hours per week in kcal[23]; all products were then summed to produce a score of daily leisure-time physical activity, subsequently expressed in sex- and centre-specific tertiles. Occupational physical activity was not evaluated in the analysis, because most participants were not working at the time of enrolment.

Anthropometric characteristics were measured in all participating centres using standardised procedures.[17] Weight was recorded to the nearest 0.1 kg and height to the nearest 0.1 or 0.5 cm. Waist circumference was measured at the either narrowest torso circumference (in Italy and in Utrecht, the Netherlands) or midway between the lower ribs and the iliac crest (in Potsdam, Germany). A combination of the above-mentioned methods was used in Greece and in Heidelberg, Germany, where waist circumference was measured at the midway between the lower ribs and the iliac crest when the narrowest circumference could not be recognised (in obese individuals). Hip circumference was measured at the widest circumference (in Italy and Greece) or over the buttocks (in Utrecht, the Netherlands and in the German centres). In Umea, Sweden, waist and hip circumferences were not measured and, therefore, these participants were excluded from analyses using waist and hip circumferences. Finally, all anthropometric measurements were adjusted to account for differences in clothing worn during measurement between the centres.

Follow-up and information on the primary end point

From the initial cohort of 30 274 elderly participants with reasonable energy intakes (participants in the top and bottom 1% of the ratio of energy intake to estimated energy requirements had already been excluded from the sample) 3478 participants (747 men and 2731 women) were excluded from all analyses because of missing values in one or more of the variables used in this analysis. After these exclusions, the final study population consisted of 27 982 elderly, 10 553 men and 17 429 women, with a mean age of 64.4 years at enrolment (minimum: 60 years, maximum: 86 years). During a median follow-up of 8 years and a total contribution of 232 639 person-years, 261 incident cases of hip fractures (203 women and 58 men) were recorded. If there was more than one hip fracture recorded for the same individual, only the first one was used in this analysis. Information on incident hip fracture was collected through active follow-up methods (telephone interviews or mailed questionnaires eliciting self-reported information) in Germany, Greece and the Netherlands, and through linkage with hospital discharge records in Italy, or hip fracture registries in Sweden, using the 10th Revision of the International Statistical Classification of Diseases (ICD-10) codes S72.0–S72.2 for hip fracture.[22] In a validation exercise conducted in Greece, 79% of self-reported cases of incident hip fractures were medically confirmed.

Statistical analysis

Frequency distributions were used for descriptive purposes. Cox proportional hazard regression was used to assess the relation of anthropometric variables (height, BMI, waist-to-hip ratio) and physical activity with incidence of hip fracture. In all proportional hazards models, follow-up time was the primary time variable and diagnosis of the first hip fracture during follow-up was the outcome event. For participants with incident hip fracture, follow-up time was calculated as the time from recruitment until diagnosis of the incident hip fracture and in a few instances death from hip fracture when hip fracture was not mentioned prior to death. For participants with no incident hip fracture, follow-up time was calculated from recruitment until the last date their vital status was assessed (by active or passive follow-up methods) or their date of death. For anthropometric variables, except for height, sex-specific quintiles were computed based on the respective frequency distributions. For height, the following five categories were used: ≤149 cm, 150–159 cm, 160–169 cm, 170–179 cm and ≥180 cm. All models were adjusted for age at recruitment (60–64 years, 65–70 years and >70 years; categorically), educational level (none, primary school completed and higher education, categorically), smoking habits (never smokers, former smokers and current smokers, categorically) and history of diabetes mellitus at enrolment (yes and no). The model with BMI as a main exposure was also adjusted for height (per 5 cm, continuous) and the model with waist-to-hip ratio as main exposure also adjusted for BMI (in

Table 1
Baseline characteristics of 27 982 participants and 261 incident hip fracture (HF) cases during follow-up, by gender. The EPIC-Elderly-NAH study.

Characteristics	Men		Women	
	Cohort (N = 10 553)	HF cases (N = 58)	Cohort (N = 17 429)	HF cases (N = 203)
	Numbers (%)			
Country				
Italy	693 (7)	1 (2)	1682 (10)	7 (4)
Netherlands	NA[†]	NA[†]	5480 (32)	83 (41)
Greece	3657 (35)	23 (40)	5208 (30)	88 (43)
Germany	4677 (44)	7 (12)	4486 (26)	11 (5)
Sweden	1526 (15)	27 (46)	573 (3)	14 (7)
Age groups (in years)				
60–64	7087 (67)	37 (64)	10 025 (57)	77(38)
65–69	2184 (21)	3 (5)	5587 (32)	78 (38)
≥70	1282 (12)	18 (31)	1817 (11)	48 (24)
Education				
Not completed primary	1370 (13)	5 (9)	3115 (18)	47 (23)
Primary school	4474 (42)	31 (53)	6821 (39)	73 (36)
Technical/professional	1789 (17)	10 (17)	3211 (19)	23 (11)
Secondary school	838 (8)	5 (9)	2833 (16)	37 (19)
Longer education	2082 (20)	7 (12)	1449 (8)	23 (11)
Height (in cm)				
≤149	21 (0.2)	1 (2)	1836 (10)	24 (12)
150–159	627 (6)	6 (10)	7693 (44)	82 (40)
160–169	4120 (39)	19 (33)	6826 (39)	74 (36)
170–179	4669 (44)	24 (41)	1048 (6)	23 (11)
≥180	1116 (11)	8 (14)	26 (0.2)	0
Body mass index (in kg/m^2)				
≤24	2710 (26)	20 (34)	53 684 (31)	77 (38)
25–29	5445 (52)	31 (53)	7120 (41)	81 (40)
≥30	2398 (23)	7 (12)	4941 (28)	45 (22)
Physical activity at leisure[*]				
Minimum (first third)	2855 (27)	20 (35)	5346 (31)	82 (40)
Moderate (second third)	3393 (32)	13 (22)	5901 (34)	71 (35)
Intense (last third)	4305 (41)	25 (43)	6182 (35)	50 (25)
Smoking status				
Never smokers	3754 (36)	25 (43)	12 368 (71)	144 (71)
Former smokers	4670 (44)	18 (31)	3220 (19)	37 (18)
Current smokers	2129 (20)	15 (26)	1841 (11)	22 (11)
History of diabetes at baseline				
No	9378 (89)	47 (81)	16 020 (92)	181 (89)
Yes	1175 (11)	11 (18)	1409 (8)	22 (11)

† Not applicable.
* A score of daily leisure-time physical activity that incorporates recreational and household activities (in gender and centre-specific tertiles).

Table 2
Cox-regression derived hazard ratios[†] (HR) for incident hip fracture with 95% confidence intervals (95% CI) in relation to anthropometric variables. The EPIC-Elderly-NAH study.

Anthropometric variables	Categories						
	1 (reference group)	2	3	4	5	Ordered categories	Continuous
Height (cm)	≤149 cm	150–159 cm	160–169 cm	170–179 cm	≥180 cm		
No. of participants	1857	8328	10 946	5717	1142		Per 5 cm
No. of cases	25	88	93	47	8		
HR (95%CI)	1	1.08 (0.68–1.72)	1.33 (0.78–2.27)	1.82 (0.96–3.45)	1.59 (0.60–4.22)	1.20 (0.99–1.45)	1.13 (1.01–1.25)
p trend						0.066	0.028
BMI (in kg/m^2)	1st quintile[*1]	2nd quintile	3rd quintile	4th quintile	5th quintile		
No. of participants	5473	5534	5621	5666	5688		
No. of cases	78	41	59	43	40		Per 1 kg/m^2
HR (95%CI)	1	058 (0.39–0.85)	0.78 (0.55–1.11)	0.56 (0.38–0.83)	0.48 (0.32–0.74)	0.85 (0.77–0.94)	0.94 (0.91–0.97)
p trend						0.001	<0.001
Waist-to-hip ratio[*2]	1st quintile[*3]	2nd quintile	3rd quintile	4th quintile	5th quintile		
No. of participants	5674	5508	4775	5552	4351		
No. of cases	56	39	36	51	38		Per 0.1
HR (95%CI)	1	0.78 (0.51–1.19)	0.96 (0.62–1.50)	1.08 (0.71–1.64)	0.87 (0.54–1.40)	1.00 (0.90–1.12)	0.97 (0.79–1.20)
p trend						0.919	0.785

† All models were stratified by gender and centre and adjusted for age at recruitment (60–64 years, 65–70 years, and >70 years; categorically), educational level (none, primary school completed and higher education, categorically), smoking habits (never smokers, former smokers and current smokers, categorically) and history of diabetes mellitus at enrolment (yes, no). Model for BMI was also adjusted for height (per 5 cm, continuous) and model for waist-to-hip ratio was also adjusted for BMI (in sex-specific quintiles, ordered) and height (per 5 cm, continuous).
[*1]For men: upper cut-off for 1st quintile: 24.5, 2nd quintile: 26.4, 3rd quintile: 28.2, and 4th quintile: 30.5.
For women: upper cut-off for 1st quintile: 23.8, 2nd quintile: 26.1, 3rd quintile: 28.5, and 4th quintile: 31.5.
[*2]Data from Umea, Sweden were not available.
[*3]For men: upper cut-off for 1st quintile: 0.92, 2nd quintile: 0.95, 3rd quintile: 0.98, and 4th quintile: 1.02.
For women: upper cut-off for 1st quintile: 0.77, 2nd quintile: 0.81 3rd quintile: 0.84, and 4th quintile: 0.89.

sex-specific quintiles, ordered) and height (per 5 cm, continuous). The model used to assess the relationship between physical activity at leisure and hip fracture incidence was also adjusted for BMI (in sex-specific quintiles, ordered) and height. All models were stratified by gender and centre and analyses were performed using STATA 8 statistical package (StataCorp. LP, College Station, TX, USA).[48]

Results

Table 1 shows baseline characteristics amongst all participants and hip fracture cases, by gender. The data in this table serve descriptive purposes because mutual confounding, time to event and country differences are not accounted for. Nevertheless, of interest is the high prevalence of overweight and obesity, amongst both men and women, as well as the high percentages of current and former smokers amongst men. Approximately 10% of the total cohort had a history of diabetes mellitus at enrolment.

Amongst women in the total cohort, mean age at menarche was 13.74 years (standard deviation (SD): 1.74) and mean age at menopause was 48.86 years (SD: 4.89). Amongst women with hip fractures, the corresponding values were 13.82 years (SD: 1.76) and 48.15 years (SD: 5.17), respectively; none of these differences were statistically significant. About 88% of women were parous, both amongst women overall and amongst those with hip fractures. Only 2% of women with hip fractures were using hormone replacement therapy at enrolment, whereas, amongst all women in the cohort, the proportion was 9%. The hazard ratio (HR) of hip fractures amongst women in comparison to men was 2.85 (95% confidence interval (CI): 1.83–4.44, $p < 0.001$) after adjustment for age at recruitment, educational level, smoking habits and history of diabetes mellitus at recruitment (results not shown).

In Table 2, Cox regression-derived HRs for incident hip fractures in relation to anthropometric variables after adjusting for other covariates are shown. The HR for a 5-cm increase in body height was 1.13 (95% CI: 1.01–1.25), whereas that for an increase by 1 kg m^{-2} of the BMI was 0.94 (95% CI: 0.91–0.97). Waist-to-hip ratio was not found to be related to hip fracture incidence (HR per 0.1: 0.97, 95% CI: 0.79–1.20).

In Table 3, Cox regression-derived HRs for incident hip fractures in relation to physical activity after adjustment for possible confounders are presented. Physical activity at leisure was inversely and statistically significantly associated with hip fracture incidence (HR per increasing tertile: 0.84, 95% CI: 0.70–0.99). The HR for participation in the intense category of the leisure-time physical activity score in comparison to lowest category was 0.71 (95% CI: 0.51–0.99).

We have further examined the association of anthropometric variables and leisure-time physical activity with hip fracture risk

Table 3
Cox-regression derived hazard ratios[†] for incident hip fracture with 95% confidence intervals (95% CI) in relation to physical activity. The EPIC-Elderly-NAH study.

Physical activity[*]	Cases (*N* = 220)	Cohort (*N* = 25 883)	Hazard ratio[†]	95% CI	*p*-value
Physical activity at leisure					
Minimum: reference group	91	7526	1		
Moderate	71	8590	0.76	0.55–1.04	0.084
Intense	58	9767	0.71	0.51–0.99	0.047
Per increasing tertile			0.84	0.70–0.99	0.039

† All models were stratified by gender and centre and adjusted for age at recruitment (60–64 years, 65–70 years, and >70 years; categorically), educational level (none, primary school completed and higher education, categorically), smoking habits (never smokers, former smokers and current smokers, categorically), BMI (in sex-specific quintiles, ordered), height (per 5 cm, continuous) and history of diabetes mellitus at enrolment (yes, no).
* Data from Umea, Sweden (2099 participants) were not included in the analysis.

by centre and we found no heterogeneity of the associations under study across the centres/cohorts included in this analysis (in all instances, the p value for heterogeneity was >0.4).

Discussion

In a prospective study of elderly Europeans, we found evidence that high body stature increased and high BMI decreased the incidence of hip fractures. Waist-to-hip ratio was not associated with hip fracture occurrence. Furthermore, increased physical activity at leisure was related to lower hip fracture incidence, independently from anthropometric characteristics.

A positive association between high body stature and hip fracture has been reported by other investigators in different populations.[7,11,15,18] Indeed, certain investigators have attributed a fraction of the increase in hip fracture incidence observed during the past decades to the increasing average stature of the population during the past century.[24] The mechanisms that have been proposed to explain this association are differences in femoral geometry and, more specifically, the longer hip axis length (the distance from the greater trochanter to the inner pelvic brim),[12,41] as well as the more substantial impact of the fall amongst taller individuals.[11] Although body height is a non-modifiable characteristic, this finding has relevance for the identification of high-risk individuals.

On the contrary, BMI was found to be inversely associated with hip fracture incidence. There is considerable evidence that indicates a beneficial effect of high BMI on bone mass[43,53] and an inverse association with hip fracture risk.[39,46] This beneficial effect is probably attributed to both fat and fat-free mass, although in postmenopausal women, fat mass has been reported to be more important.[43] Several underlying mechanisms have been proposed. Both fat and fat-free mass increase mechanical load and stimulate bone remodelling.[47] In postmenopausal women, fat mass is an important source of oestrogens that suppress osteoclast function.[36] Moreover, in obese individuals, high blood insulin levels may contribute to overproduction of sex hormone levels, which reduce osteoclast and increase osteoblast activity.[53] Leptin, an adipocyte-secreted hormone, which is positively associated with BMI, has also been reported to play a role, although complex, in the relation between body fat and fracture risk, with predominantly beneficial effects on the skeleton.[10,43] Furthermore, adipose tissue can act as a protective 'cushion' against trauma during a fall, especially in the hip region. Excessive fat mass, however, may not protect against osteoporotic fractures.[19,52,53] From a recent meta-analysis from almost 60 000 men and women from 12 prospective population-based cohort studies, it was concluded that it is the very low BMI, which is associated with increased risk for hip fractures.[8] Our data are not in line with this finding because participants with very low BMI (below 20 kg m^{-2}) had no greater risk of hip fractures compared with those within the normal ranges (between 20 and 25 kg m^{-2}) of BMI (results not shown). Nevertheless, as a conclusion, a reasonable public health message for the prevention of these age-related fractures is the avoidance of very low body weight.[9]

Central fat distribution, as reflected anthropometrically by the waist-to-hip ratio, was not associated with hip fracture risk in this population. Relatively few studies have explored the relation of abdominal obesity, mainly as one of the components of metabolic syndrome, with hip fracture risk, and have pointed to a positive association.[13,51] Furthermore, the evidence regarding the association of central obesity with bone mass density is so far inconclusive. Thus, in individuals with metabolic syndrome, characterised by predominant central obesity, the beneficial effect of obesity *per se* can be counterbalanced by the systemic inflammation caused by the syndrome itself.[20,31,49,51]

There is considerable evidence from observational epidemiological studies that physical activity is beneficial for the prevention of hip fractures.[3,14,32,34,40] In a recent meta-analysis, moderate to vigorous physical activity was found to be associated with substantial reduction in hip fracture risk in both genders.[40] The beneficial effect of physical activity has been attributed to the maintenance or even improvement of muscular mass and strength, as well as of body balance and physical function.[30] Regular lifetime physical activity, notably weight-bearing and resistance activities, tends to increase peak bone mass in youth and maintain high bone mass in later life by increasing the mechanical load and promoting bone remodelling.[14,19] Our data support a substantial inverse dose–response relationship between leisure-time physical activity and hip fracture risk.

The strengths of our investigation are its prospective design, the relatively long follow-up and the employment of validated research instruments including those focussing on physical activity.[42] The physical activity assessment questionnaire was developed and validated in relatively younger persons and this may imply increased non-differential misclassification amongst older individuals. This type of misclassification, however, cannot generate an association when none exists and can only attenuate an existing one. An important limitation of our investigation is that fractures even as important as hip fractures may not be always reported, particularly in centres that rely on active follow-up. This would create underestimation of the incidence of fractures and of the incidence attributable to various exposures. However, the ratio of the incidence rates amongst exposed and unexposed will not be affected unless underreporting is associated with a particular exposure. This could not happen in the study design used in the present study.[35] It is also possible that underreporting would be different amongst centres and this could create confounding bias. In our analysis, however, we have stratified for centre and this controls for any possible confounding. The study samples are not strictly representative of the underlying general population groups because they are limited to volunteers, as they should. However, representativeness is not a prerequisite for validity in cohort studies although it may explain the relative low incidence of hip fractures in our study. Other limitations are the relatively few number of outcomes, in particular at the extreme categories of the exposure distributions (e.g., very thin or very obese participants), and the different sources of information related to hip fracture incidence amongst the centres. Nevertheless, the accuracy of the self-reported hip fractures is generally considered high and more reliable compared with other fracture sites because people are almost always hospitalised and more likely to report them correctly.[4,21] Moreover, there could not be differential misclassification of self-reported hip fractures by level of the evaluated exposure variables, and differences in the completeness of reporting amongst centres, as indicated, were addressed in the analysis through stratification by centre. Finally, in the majority of the centres, information on the mechanism of hip fracture occurrence was not available to discern low- from high-energy trauma fractures.

Conclusions

In conclusion, in a population of elderly Europeans followed up for approximately 8 years, we have found evidence that body height is associated with increased, whereas BMI with decreased hip fracture incidence. Physical activity at leisure, defined as a measure combining recreational and household activities, appears to be beneficial for the prevention of hip fractures.

Conflict of interest statement

There are none.

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References

1. Benetos IS, Babis GC, Zoubos AB, et al. Factors affecting the risk of hip fractures. Injury 2007;38:735–44.
2. Centre JR, Nguyeen TV, Schneider D, et al. Mortality after all types of osteoporotic fracture in men and women: an observational study. Lancet 1999;353: 878–82.
3. Chan BK, Marshall LM, Winters KM, et al. Incident fall risk and physical activity and physical performance among older men: the Osteoporotic Fractures in Men Study. Am J Epidemiol 2007;165:696–703.
4. Chen Z, Kooperberg C, Pettinger MB, et al. Validity of self-report for fractures among a multi-ethnic cohort of postmenopausal women: results from the women' health Initiative observational study and clinical trials. Menopause 2004;11:264–74.
5. Cooper C, Campion G, Melton LJ. Hip fractures in the elderly: a world wide projection. Osteopor Int 1992;2:285–9.
6. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet 2002;359:1761–7.
7. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. N Engl J Med 1995;332:767–73.
8. De Laet C, Kanis JA, Odén A, et al. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int 2005;16(11):1330–8.
9. Diet, nutrition and the prevention of chronic diseases. Report of a joint WHO/FAO Expert Consultation. Geneva: World Health Organization; 2003(WHO Technical Report Series, No. 916).
10. Ducy P, Amling M, Takeda S, et al. Leptin inhibits bone formation through a hypothalamic relay: a central control of bone mass. Cell 2000;100:197–207.
11. Farahmand BY, Michaëlsson K, Baron JA, et al. Body size and hip fracture risk. Swedish Hip Fracture Study Group. Epidemiology 2000;11:214–9.
12. Faulkner KG, Cummings SR, Black D, et al. Simple measurement of femoral geometry predicts hip fracture: the study of osteoporotic fractures. J Bone Miner Res 1993;8(10):1211–7.
13. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160(14):2117–28.
14. Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: a review of the epidemiologic evidence. J Am Geriatr Soc 2000;48:883–93.
15. Gunnes M, Lehmann EH, Mellstrom D, Johnell O. The relationship between anthropometric measurements and fractures in women. Bone 1996;19(4):407–13.
16. Haftenberger M, Schuit AJ, Tormo MJ, et al. Physical activity of subjects aged 50–64 years involved in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 2002;5(6B):1163–76.
17. Haftenberger M, Lahmann PH, Panico S, et al. Overweight, obesity and fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public Health Nutr 2002;5(6b): 1147–62.
18. Hemenway D, Feskanich D, Colditz GA. Body height and hip fracture: a cohort study of 90 000 women. Int J Epidemiol 1995;24(4):783–6.
19. Hsu YH, Venners SA, Terwedow HA, et al. Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. Am J Clin Nutr 2006;1:146–54.
20. Hwang DK, Choi HJ. The relationship between low bone mass and metabolic syndrome in Korean women. Osteoporos Int 2010. doi:10.1007/s00198-009r-r0990-2.
21. Ismail AA, O'Neill TW, Cockerill W, et al. Validity of self-report of fractures: results from a prospective study in men and women across Europe. EPOS Study Group. European Prospective Osteoporosis Study Group. Osteoporos Int 2000;11(3):248–54.
22. ICD-10: 10th International Statistical Classification of Diseases and related health problems: tenth revision, 2nd ed., Geneva: World Health Organization; 2004.
23. James WPT, Schofield EC. Human energy requirements: a manual for planners and nutritionists. Oxford/New York/Tokyo: Oxford University Press; 1990 .
24. Joakinmsen RM, Fonnebo V, Magnus JH, et al. The Tromso study: body height, body mass index and fractures. Osteoporos Int 1998;8:436–42.
25. Johnell O. The socioeconomic burden of fractures: today and in the 21th century. Am J Med 1997;103:S20–5.
26. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. Osteoporos Int 2005;16(Suppl. 2):S3–7.
27. Kanis JA, Borgstrom F, De Laet C, et al. Assessment of fracture risk. Osteoporos Int 2005;16(6):581–9.
28. Kanis JA, Burlet N, Cooper C, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2008;19(4):399–428.
29. Kannus P, Parkkari J, Sievanen H, et al. Epidemiology of hip fractures. Bone 1996;18:57S–63S.
30. Kannus P, Uusi-Rasi K, Palvanen M, Parkkari J. Non-pharmacological means to prevent fractures among older adults. Ann Med 2005;37:303–10.
31. Kinjo M, Setoguchi S, Solomon DH. Bone mineral density in adults with the metabolic syndrome: analysis in a population-based U.S. sample. J Clin Endocrinol Metab 2007;92(11):4161–4.
32. Kujala UM, Kaprio J, Kannus P, et al. Physical activity and osteoporotic hip fracture risk in men. Arch Intern Med 2000;160:705–8.
33. Lau EMC, Cooper C. The epidemiology of osteoporosis: the oriental perspective in a world context. Clin Orthop 1996;323:65–74.
34. Layne JE, Nelson ME. The effects of progressive resistance training on bone density: a review. Med Sci Sports Exerc 1999;31(1):25–30.
35. MacMahon B, Trichopoulos D. Cohort studies. In: MacMahon B, Trichopoulos D, editors. Epidemiology: principles and methods. 2nd ed., Boston: Little Brown and Company; 1996. p. 184–5.
36. Michael H, Härkönen PL, Väänänen HK, Hentunen TA. Estrogen and testosterone use different cellular pathways to inhibit osteoclastogenesis and bone resorption. J Bone Miner Res 2005;20:2224–32.
37. Melton 3rd LJ. Hip fractures: a worldwide problem today and tomorrow. Bone 1993;14:1–8.
38. Melton 3rd LJ. Epidemiology of hip fractures: implications of the exponential increase with age. Bone 1996;18:S121–5.
39. Meyer HE, Tverdal A, Falch JA. Body height, body mass index, and fatal hip fractures: 16 years' follow-up of 674 000 Norwegian women and men. Epidemiology 1995;6(3):299–305.
40. Moayyeri A. The association between physical activity and osteoporotic fractures: a review of the evidence and implications for future research. Ann Epidemiol 2008;18(11):827–35.
41. Nankaku M, Kanzaki H, Tsuboyama T, Nakamura T. Evaluation of hip fracture risk in relation to fall direction. Osteoporos Int 2005;16(11):1315–20.
42. Pols MA, Peeters PH, Ocké MC, et al. Estimation of reproducibility and relative validity of the questions included in the EPIC Physical Activity Questionnaire. Int J Epidemiol 1997;26:S181–9.
43. Reid IR. Relationships between fat and bone. Osteporosis Int 2008;19: 595–606.
44. Riboli E, Hunt KJ, Slimani N, et al. European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr 2002;5:1113–24.
45. Richmond J, Aharonoff GB, Zucherman JD, Koval KJ. Mortality risk after hip fracture. J Orthop Trauma 2003;17:53–6.
46. Robbins J, Aaron K, Aragaki MS, et al. Factors associated with 5-year risk of hip fracture in postmenopausal women. JAMA 2007;298(20):2389–98.
47. Skerry TM. The response of bone to mechanical loading and disuse: fundamental principles and influences on osteoblast/osteocyte homeostasis. Arch Biochem Biophys 2008;473(2):117–23.
48. Stata Corporation 2003 STATA 8.0 intercooled. TX, USA: StataCorp.; 2003.
49. Tarquini B, Navari N, Perfetto F, et al. Evidence for bone mass and body fat distribution relationship in postmenopausal obese women. Arch Gerontol Geriatr 1997;24(1):15–21.
50. Trichopoulou A, Bamia C, Norat T, et al. Modified Mediterranean diet and survival after myocardial infarction: the EPIC-Elderly study. Eur J Epidemiol 2007;22:871–81.
51. von Muhlen D, Safii S, Jassal SK, et al. Associations between the metabolic syndrome and bone health in older men and women: the Rancho Bernardo Study. Osteoporos Int 2007;18(10):1337–44.
52. Wardlaw GM. Putting body weight and osteoporosis into perspective. Am J Clin Nutr 1996;63:433S–6S.
53. Zhao LJ, Liu YJ, Liu PY, et al. Relationship of obesity with osteoporosis. J Clin Endocrinol Metab 2007;92:1640–6.