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ORIGINAL ARTICLE

Coffee, tea and caffeine consumption in relation to osteoporotic fracture risk in a cohort of Swedish women

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Abstract *Introduction:* Consumption of coffee and tea, and total intake of caffeine has been claimed to be associated with osteoporotic fracture risk. However, results of earlier studies lack consistency. *Methods:* We examined this relation in a cohort of 31,527 Swedish women aged 40-76 years at baseline in 1988. The consumption of coffee, caffeinated tea and the intake of caffeine were estimated from a self-administered food frequency questionnaire (FFQ). Multivariate-adjusted hazards ratios (HRs) of fractures with 95% confidence intervals (95% CIs) were estimated by Cox proportional hazards models. *Results:* During a mean follow-up of 10.3 years, we observed 3,279 cases with osteoporotic fractures. The highest (>330 mg/day) compared with the lowest (<200 mg/day) quintile of caffeine intake was associated with a modestly increased risk of fracture: HR 1.20 (95% CI: 1.07–1.35). A high coffee consumption significantly increased the risk of fracture (p for trend 0.002), whereas tea drinking was not associated with risk. The increased risk of fracture with both a high caffeine intake and coffee consumption was confined to women with a low calcium intake (<700 mg/day): HR 1.33 (95% CI: 1.07–1.65) with ≥4 cups (600 ml)/day of coffee compared to <1 cup (150 ml)/day. The same comparison but risk estimated for women with a high propensity for fractures (≥2 fracture types) revealed a HR of 1.88 (95% CI: 1.17–3.00). *Conclusions:* In conclusion, our results indicate that a daily intake of 330 mg of caffeine, equivalent to 4 cups (600 ml) of coffee, or more may be associated with a modestly increased risk of osteoporotic fractures, especially in women with a low intake of calcium.

Keywords Caffeine · Coffee · Cohort study · Fracture · Tea

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Introduction

Osteoporotic fractures will affect at least half of all white women older than 50 years and these types of fractures are therefore considered a major health problem in many countries [1].

In addition to tremendous public health costs, the consequences of an osteoporotic fracture for an individual are often severe. The patient may encounter long-lasting health problems such as immobility and pain, which may result in a loss of life quality and even in increased mortality risk [2, 3].

Several modifiable risk factors, including diet, are considered to be important for osteoporotic fractures [4–6]. Among the proposed dietary factors, high consumption of caffeine-containing beverages such as coffee and tea is hypothesized to be associated with increased risk.

Caffeine has been reported to increase urinary calcium excretion [7] and it has also been suggested that caffeine decreases intestinal calcium absorption efficiency [8]. These mechanisms might promote a negative calcium balance, which can be of importance for bone loss, especially when intake of caffeine is high and ingestion and absorption of calcium is low [9].

The clinical impact of a high caffeine intake on fracture risk has previously been evaluated, but results from earlier investigations have been inconsistent. The majority has not observed any association with hip fractures [10–20] or other osteoporotic fractures like fractures affecting the forearm [12, 21], spine [13] and wrist [13]. Accordingly, only a few epidemiological studies have found a statisti-

cally significant association between high consumption of caffeine and an increased risk of hip fractures [21–24] or fractures of the wrist [12]. However, only one previous study [24] has considered the conceivable modifying effect of calcium intake on the risk of fracture associated with a high consumption of caffeine even though this interaction has been suggested in a study with bone mineral density as outcome [25].

Regarding tea, both a decreased risk of osteoporotic fractures [17, 20] and a decreased risk of low bone mineral density (BMD) have been reported [26–28].

The Swedish population, like the populations in the other Nordic countries, has a high consumption of coffee per capita in an international comparison, whereas the intake of tea is generally low [29]. In Sweden the per capita consumption of roasted coffee reached over 11 kg in 1976 and then declined to approximately 9 kg in 2004 [29, 30]. In most other countries, except for Finland, the per capita consumption is lower than in Sweden, for example 3.3, 4.4 and 7.1 kg in Ireland, France and the Netherlands, respectively [30]. In the United States the per capita consumption of roasted coffee was 4.5 kg in 1994 [29]. In this context it should be stressed that volumes of cups can vary considerably between different countries, as also the types of coffee used, dosages and preparation methods, which are likely to introduce uncertainty when comparing consumption patterns between countries.

Since a substantial proportion of the Swedish population are high consumers of coffee (and thus caffeine), this country should be an appropriate setting to study the relationship between coffee and caffeine and risk of osteoporotic fractures.

The principal aim of this study was to investigate the association between consumption of coffee, caffeinated tea and caffeine intake and the risk of incident osteoporotic fractures in a large prospective population-based cohort of Swedish women, 40–76 years old at the start of the study. A secondary aim was to evaluate whether the level of dietary calcium influenced these fracture risk estimates.

Methods

All women born between 1914 and 1948 and resident in the Uppsala county (n=48,517) were invited by mail to participate in a mammography screening between January 1988 and December 1990. A six-page questionnaire on demographic and lifestyle factors was enclosed with the invitation. The following factors were included in the questionnaire: height (cm), weight (kg), marital status, parity, age at first birth and education. In addition to the general questions, the women were asked to respond to a food frequency questionnaire (FFQ). The proportion of women who returned a completed questionnaire was 72% (n=34,916). Women were excluded from the study if they had missing or incorrect ID numbers, did not fall within the age range of 40–76 years at the time of filling in the questionnaire, had a missing return date on the questionnaire, moved out of the study area or had died during follow-up but for whom the date of death was missing. Furthermore, women with extreme energy intake estimates (below or above mean 3 standard deviations for logarithmic transformed calories) were excluded from the analysis. Women were also excluded if they had reported extremely unreasonable values for height and weight, or if they had, after matching to the Swedish Cancer Registry, prevalent cancers at study entry. Thus, the final sample comprised 31,527 women.

Dietary assessment

The FFQ included questions on 67 food items commonly eaten in Sweden. The participants were asked how often on average per day they had consumed these food items during the past 6 months. Questions on consumption of regular coffee and black tea were included in the FFQ. It should be noted that decaffeinated coffee and tea are not typically consumed in the Swedish diet. The major method of preparation of coffee is brewing, not cooking. The caffeine content is higher in brewed coffee than in percolated coffee [29]. The main caffeine sources being assessed in this FFQ were coffee, tea, caffeinated soft drinks and chocolate. No information about supplements or medicines containing caffeine was obtained. Eight predefined frequency categories were used that ranged from "never/seldom" to "four times or more per day". Additional open questions regarding consumption of dairy products were included (number of slices of cheese per day, type of milk and number of glasses of milk per day). For nutrient calculations, age-specific portion sizes were used (40–52, 53–65, ≥66 years) based on mean values of 5,922 days of weighed food records from 213 women participating in the validation of the FFQ. Caffeine, alcohol and nutrient intake (such as calcium, phosphorous, vitamins D and A) and energy intake were computed by multiplying the frequency of consumption of each unit of food by the nutrient content of specified portions derived from a database created by the Swedish National Administration [31]. Consumption of one cup (150 ml) of coffee corresponded to an intake of 80 mg of caffeine.

The validity of the nutrient estimates based on self-reported food frequencies was evaluated in a subsample of 129 women from the cohort. Each of the 129 participants weighed and recorded all consumed foods and beverages during four 7-day periods 3–4 months apart. The validity of coffee and tea estimates from the FFQ assessed by Spearman's correlation coefficient between the FFQ and food records was r=0.6 and 0.8 respectively.

The mean energy intake in the subsample used for validation was 1,692 (±349) kcal, and mean body mass index was 24.77 (±3.72) kg/m^2. In the whole cohort corresponding values were 1,330 (±376) kcal and 24.74 (±3.93) kg/m^2.

Identification of fracture cases and follow-up of the cohort

All types of fracture considered typical osteoporotic fractures [32] were identified in women in the county of Uppsala. These involve all fractures of the proximal femur, i.e. hip fractures, fractures of the pelvis, spine, distal forearm and proximal humerus. Fracture cases in the study cohort were identified by matching the unique personal identification number of the study participants with the local outpatient registers, hospital discharge records and X-ray records from January 1988 through December 2000. The registers at the three hospitals of the Uppsala county and the two primary care centers with X-ray equipment were used. In addition, the ascertainment of hip fracture cases was completed by use of the nationwide Swedish inpatient register. In this register all hospital admissions in the Uppsala county have been reported since 1964. The validity of the fracture register data is high with an accuracy of 99% [33, 34]. Women identified as having had a fracture of the hip, distal forearm, pelvis, spine or proximal humerus before study entry were excluded; thus only women with a first-incident fracture were included in the analyses. Fractures that were due to high-energy trauma were retained in the analysis because there are indications of a comparable increased low and high trauma fracture risk with decreasing bone density in the elderly [35]. Pathologic fractures that were due to cancer, unfortunately, could not be excluded if they had erroneously been coded as a traumatic fracture in that we did not have the possibility to identify these cases, though we did exclude women with prevalent cancers. However, the proportion of fractures with these causes is low, being approximately 1% in comparison with those that are due to low-energy trauma.

Statistical analyses

Cox proportional hazards models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) measuring the association between exposure and the occurrence of osteoporotic fractures. Person-years were calculated for each woman from the date of entry into the cohort to the date of death, the date of migration from the study area or to the end of the follow-up period (31 December 2000). The women were grouped into four categories of consumption: <1 cup/day, 1 cup/day, 2–3 cups/day and 4 cups (600 ml) or more per day for coffee and for tea consumption, and quintiles of caffeine intake. To examine the linear trend the exposure variables were entered into the models as consecutive integers of the four coffee and tea categories, respectively, and the five caffeine categories.

The basic model used to estimate HRs included age at study entry divided into 5-year age groups. In a multivar-

Table 1 Baseline characteristics of the study cohort by amount of coffee consumption (1 cup of coffee is assumed to contain 150 ml)

Coffee consumption				
	<1 cup/day (*n*=2,520)	1 cup/day (*n*=4,128)	2–3 cups/day (*n*=18,703)	≥4 cups/day (*n*=5,887)
Person-years	25,636	41,693	193,950	61,872
	Mean ±SD			
Age at baseline (years)	53.9±10.4	57.5±10.6	54.6±10.0	50.0±8.2
Calcium intake (mg/day)	692±218	704±203	701±189	708±191
Vitamin D intake (μg/day)	3.17±1.10	3.25±1.02	3.29±1.00	3.30±1.03
Vitamin A intake (mg/day)	0.90±0.56	0.89±0.44	0.90±0.42	0.92±0.50
Energy intake (kcal/day)	1254±386	1255±359	1333±356	1399±402
Weight (kg)	66.4±12.0	66.6±11.3	66.6±10.7	66.7±11.2
Height (cm)	164.2±6.1	163.9±5.8	164.2±5.8	164.7±5.8
Body mass index (kg/m^2)	24.6±4.3	24.8±4.07	24.7±3.8	24.6±3.9
	n (%)			
Education				
Low (≤12 years)	1,709 (68)	3,103 (75)	14,318 (77)	4,405 (75)
High (<12 years)	811 (32)	1,025 (25)	4,385 (23)	1,482 (25)
Marital status				
Married/cohabitant	1,692 (67)	2,838 (69)	14,065 (75)	4,460 (76)
Single/widow	828 (33)	1,290 (31)	4,647 (25)	1,427 (24)
Children				
0	366 (15)	614 (15)	2,133 (11)	524 (9)
1	411 (16)	708 (17)	2,999 (16)	929 (16)
2	887 (35)	1,427 (35)	7,409 (40)	2,362 (40)
3	527 (21)	879 (21)	4,104 (22)	1,374 (23)
4	195 (8)	325 (8)	1,360 (7)	460 (8)
5+	134 (5)	175 (4)	698 (4)	238 (4)

iate model we further included height, weight, intake of vitamin D, vitamin A, calcium, phosphorus, alcohol and energy (all continuous), educational level (low vs high) and marital status (married or cohabitant vs single or widowed). Parity and age at first birth were not included in the model, as they did not influence the estimates more than marginally.

Because an effect modification by calcium had been indicated in an earlier study of caffeine intake and bone density [9], interactions were examined by inclusion in the model of product terms between the respective exposures and calcium intake. Fracture risk associated with the exposures was then separately estimated in a low and a high calcium group stratified by the mean dietary calcium intake (700 mg/day) of the cohort.

To obtain a more limitless view of the shape of the association between consumption of caffeine and the risk of osteoporotic fractures a restricted Cox's regression spline line model was also applied [36]. The knots in the spline analysis are 105, 210 and 341 mg caffeine, which are equivalent to the 10, 50 and 90 percentiles, respectively. The results of this analysis are presented as a smoothed plot with 95% CIs. All analyses were done using SAS version 8.02 (SAS Institute Inc, Cary, NC, USA).

Results

Fractures during follow-up

During an average of 10.3 years of follow-up and a total of 321,151 person-years, we observed 3,279 cases with first osteoporotic fractures at any fracture site, which equals a cumulative average incidence of 1% of the women having had a fracture per year. Of these osteoporotic fractures, 880 were found to be fractures of the hip. In addition, 524 women with a fracture of the pelvis, 405 with a vertebral fracture, 1,972 with a distal forearm fracture and 633 with a fracture of the proximal humerus were identified. At the event of fracture, the mean age of the women was 67.2 years with a median of 68.4 years. Characteristics of the participants are presented in Table 1.

Coffee

The consumption of coffee in this cohort was high since approximately 59% of the participants reported a consumption of 2–3 cups of coffee daily and about 19% reported a daily intake of 4 cups (600 ml) of coffee or more. A statistically significant linear trend (Table 2) for an increased risk of all fractures with increasing coffee drinking was observed (p for trend 0.002). The trend was also significant when we excluded hip fracture cases from the analyses (p=0.02). Nevertheless, a nonlinear risk was indicated by the significant inclusion of a quadratic term (p=0.01) of daily coffee consumption, together with coffee as an ordinary continuous term in the multivariate model. The increase in risk was mainly confined to those women who consumed 4 cups of coffee per day or more. Inclusion of tea consumption in the multivariate model did not more than marginally affect our estimates for coffee.

We observed that the association between coffee consumption and fracture risk was modified by calcium intake: the p value for interaction was 0.02. The multivariate p value for trend of fracture risk with coffee intake in women below the estimated average calcium intake of 700 mg/day was 0.002; for women with an estimated higher calcium intake, the multivariate p value for trend was 0.18. Those drinking 4 cups of coffee or more per day

Table 2 Coffee consumption at baseline 1988–1990, hazards ratios (HRs) and 95% confidence intervals (95% CIs) of osteoporotic fracture in 31,527 women (1 cup of coffee is assumed to contain 150 ml)

	<1 cup/day	1 cup/day	2–3 cups/day	4+ cups/day	p for trend
Number of cases	255	504	2,024	508	
Number of person-years	25,704	41,949	194,537	62,050	
Age-adjusted HR (95% CI)	1.0 (ref)	0.96 (0.82–1.12)	1.01 (0.89–1.15)	1.15 (0.99–1.34)	0.03
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	0.97 (0.83–1.14)	1.06 (0.92–1.21)	1.22 (1.04–1.43)	0.002
Calcium intake (<700 mg/day)					
Number of cases	132	256	1038	269	
Number of person-years	14,120	22,356	102,920	30,896	
Age-adjusted HR (95% CI)	1.0 (ref)	0.97 (0.79–1.21)	1.03 (0.86–1.24)	1.27 (1.03–1.57)	0.01
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	0.96 (0.77–1.20)	1.07 (0.89–1.29)	1.33 (1.07–1.65)	0.002
Calcium intake (≥700 mg/day)					
Number of cases	123	248	986	239	
Number of person-years	11,583	19,593	91,617	31,154	
Age-adjusted HR (95% CI)	1.0 (ref)	0.94 (0.76–1.17)	0.99 (0.82–1.19)	1.04 (0.83–1.30)	0.52
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	0.98 (0.78–1.24)	1.05 (0.86–1.29)	1.13 (0.89–1.42)	0.18

*Hazard ratios and 95% confidence intervals are adjusted for age at study entry (in 5-year categories), height, weight, total caloric intake, vitamin D intake, vitamin A intake, calcium intake, phosphorous intake, alcohol intake (all continuous), education (low vs high), marital status (married or cohabitant vs single or widowed)

compared to less than 1 cup/day in the low calcium intake subcohort had a HR of 1.33 (95% CI: 1.07–1.65). When the same comparison was done within the high calcium consumers, the HR was found to be 1.13 (95% CI: 0.89–1.42). If we restricted the analyses to cases who had sustained two or more fracture types (i.e. those with higher propensity of fractures, n=736), the corresponding HR was further strengthened in the low but not in the high calcium intake group: HR 1.88 (95% CI: 1.17–3.00) and HR 0.89 (95% CI: 0.53–1.45).

Tea

We found no statistically significant associations between consumption of tea and incidence of osteoporotic fractures (Table 3). Moreover, no significant interaction with calcium intake was observed (p value for interaction 0.25) and the results, therefore, remained similar after stratification by calcium intake (data not shown).

Caffeine

Because the major source of caffeine intake is coffee (Spearman's correlation coefficient=0.8), we also expectedly found (Table 4) an increased risk of fracture with a high caffeine intake (multivariate p for trend 0.008). Women in the highest quintile of caffeine intake (median intake 350 mg/day) compared with women in the lowest quintile of intake (median intake 100 mg/day) had a statistically significant increased risk of fracture 1.20 (95% CI: 1.07–1.35). When we stratified the cohort by calcium intake (p for interaction 0.07 between caffeine and calcium intake), the increased risk for any osteoporotic fracture was statistically significant only when the calcium intake was low (<700 mg/day). In this case, the multivariate-adjusted HR of highest compared with lowest quintile of caffeine intake was 1.28 (1.09–1.50), with a tendency of an increased risk also in quintile 4. The overall trend was found to be statistically significant (p=0.003), whereas no significant trend towards an increased risk with higher caffeine intake was observed in those with a high calcium intake. We furthermore restricted the analyses to women with two fracture types or more during follow-up. Among those with a low calcium intake, women within the highest caffeine intake quintile compared to the lowest quintile conferred a HR of 1.49 (95% CI: 1.13–1.96), whereas the same comparison among women with higher calcium consumption gave a HR of 1.01 (95% CI: 0.73–1.39).

In an effort to describe the unrestricted relationship between intake of caffeine and the risk of fractures a multivariate cubic spline Cox's regression analysis with 80 mg caffeine (equivalent to approximately 1 cup of coffee) intake level as a fixed reference was carried out. The smoothed exposure-effect curve shown in Fig. 1 indicates that the risk of osteoporotic fractures is significantly increased by an intake between approximately 300 and 350 mg caffeine daily or higher corresponding to the highest quintile of caffeine intake in this cohort or 4 cups (600 ml) or coffee or more.

Discussion

In this large prospective cohort of Swedish women a daily intake of caffeine equivalent to approximately 4 cups (600 ml) of coffee or more was associated with a significantly increased risk of osteoporotic fractures. This association was only apparent when the calcium intake was low and especially pronounced for women who had higher propensity for fractures, i.e., two osteoporotic fracture types or more. In contrast, no statistically significant association was observed for caffeinated tea in relation to fracture risk.

Previous fracture studies

Studies that have examined an association between consumption of coffee and intake of caffeine and risk of osteoporotic fractures have indicated conflicting results. An association between intake of coffee or caffeine and increased risk of osteoporotic fractures in general or hip fractures specifically was found in some cohort studies [21–24], whereas a positive association with wrist fractures was found in only one study [12].

Kiel et al. [22] studied the intake of caffeine in relation to the risk of hip fracture in the Framingham cohort. The study population consisted of 3,170 men and women (aged 50–84 years). Hip fractures were reported in 135 individuals during the 12-year follow-up. Intake of ≥2.5

Table 3 Tea consumption at baseline 1988–1990, hazards ratios (HRs) and 95% confidence intervals (95% CIs) of osteoporotic fracture in 31,527 women (1 cup of tea is assumed to contain 200 ml)

	<1 cup/day	1 cup/day	2–3 cups/day	4+ cups/day	p for trend
Number of cases	2,017	835	231	16	
Number of person-years	198,518	85,977	26,842	2,605	
Age-adjusted HR (95% CI)	1.0 (ref)	0.97 (0.90–1.06)	1.01 (0.88–1.16)	0.85 (0.52–1.39)	0.64
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	0.96 (0.89–1.05)	0.97 (0.84–1.11)	0.80 (0.48–1.33)	0.28

*Hazard ratios and 95% confidence intervals are adjusted for age at study entry (in 5-year categories), height, weight, total caloric intake, vitamin D intake, vitamin A intake, calcium intake, phosphorous intake, alcohol intake (all continuous), education (low vs high), marital status (married or cohabitant vs single or widowed)

Table 4. Quintiles of caffeine consumption at baseline 1988–1990, hazards ratios (HRs) and 95% confidence intervals (95% CIs) of osteoporotic fracture in 31,527 women

	Quintiles of daily caffeine intake (mg/day)					
	1 <200	2 200–209	3 210–249	4 250–329	5 >329+	*p* for trend
Number of cases	710	715	673	598	614	
Number of person-years	60,207	59,251	68,155	63,162	74,268	
Median intake (mg/day)						
Age-adjusted HR (95% CI)	1.0 (ref)	1.02 (0.92–1.13)	0.97 (0.88–1.08)	1.03 (0.92–1.15)	1.15 (1.03–1.28)	0.03
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	1.06 (0.95–1.18)	1.00 (0.90–1.12)	1.06 (0.95–1.19)	1.20 (1.07–1.35)	0.008
Calcium intake (<700 mg/day)						
Number of cases	363	370	321	329	319	
Number of person-years	32,495	31,819	35,591	33,912	37,006	
Age-adjusted HR (95% CI)	1.0 (ref)	1.03 (0.89–1.20)	0.91 (0.79–1.07)	1.11 (0.96–1.29)	1.24 (1.06–1.45)	0.008
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	1.07 (0.92–1.24)	0.96 (0.82–1.12)	1.16 (0.99–1.35)	1.28 (1.09–1.50)	0.003
Calcium intake (≥700 mg/day)						
Number of cases	347	345	352	269	295	
Number of person-years	27,712	27,432	32,564	29,249	37,261	
Age-adjusted HR (95% CI)	1.08 (ref)	1.03 (0.88–1.19)	1.04 (0.89–1.21)	0.96 (0.81–1.12)	1.08 (0.92–1.27)	0.66
Multivariate-adjusted HR* (95% CI)	1.0 (ref)	1.06 (0.91–1.24)	1.06 (0.91–1.24)	0.98 (0.82–1.15)	1.13 (0.96–1.34)	0.40

*Hazard ratios and 95% confidence intervals are adjusted for age at study entry (in 5-year categories), height, weight, total caloric intake, vitamin D intake, vitamin A intake, calcium intake, phosphorous intake, alcohol intake (all continuous), education (low vs high), marital status (married or cohabitant vs single or widowed

units of caffeine/day (1 cup of coffee=1 unit of caffeine; corresponding amount in mg not stated) was found to significantly increase the risk of hip fractures (RR: 1.69, 95% CI: 1.05–2.74) in comparison with a intake of 0–1 units of caffeine per day. The increased risk was mainly concentrated to women aged 65 years or older. The investigators focused only on caffeine and did not consider the exposure to coffee and tea separately. As some studies have indicated that tea could exert a protective effect on BMD [26–28], it is possible that this could influence the interpretation of the results. Data by dietary calcium were not presented.

In the Nurses Health Study [21] 84,484 women were studied over a 6-year period regarding any associations between intake of caffeine and consumption of coffee, tea and cola drinks and fractures of the hip or the forearm. During the 6-year follow-up, 65 cases of hip fractures were reported. A significantly elevated risk of hip fracture (RR: 2.95, 95% CI: 1.18–7.38) was found in women consuming ≥817 mg caffeine per day in comparison with those consuming <192 mg/day. The consumption of >4 cups of

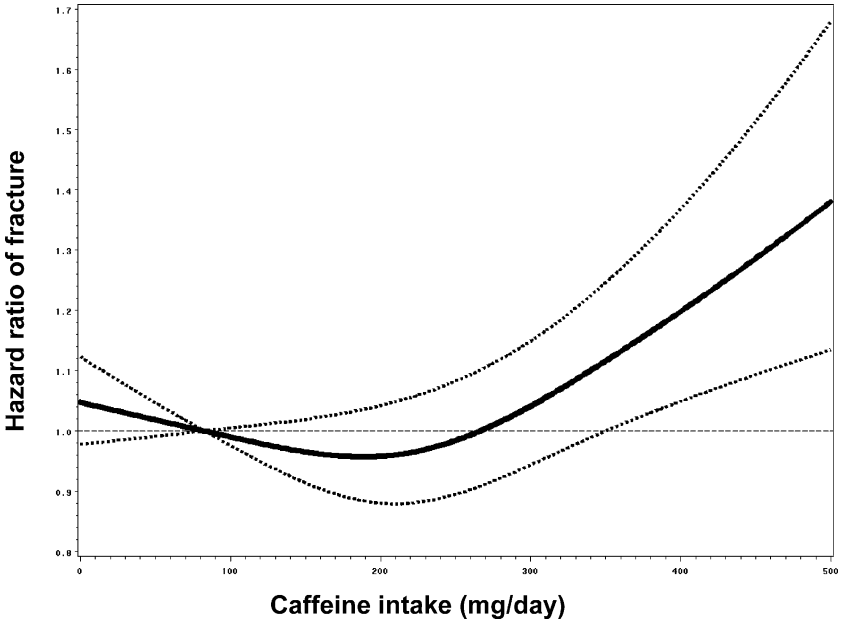

Fig. 1 Multivariate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) (*narrow lines*) of any osteoporotic fracture by dietary caffeine intake. The smoothed curve was fitted with a restricted cubic Cox's regression spline model with a caffeine intake of 80 mg/day, corresponding to approximately 1 cup of coffee (corresponding to 150 ml) as the reference. The model included age at study entry (in 5-year categories), height, weight, total caloric intake, vitamin D intake, vitamin A intake, calcium intake, phosphorous intake, alcohol intake (all continuous), education (low vs high) and marital status (married or cohabitant vs single or widowed)

coffee/day versus 0 cups of coffee/day resulted in a relative risk of hip fracture of 3.35 (95% CI: 1.32–8.49). Even though 593 fractures of the forearm were included in the analysis, no increased risk in relation to caffeine or coffee was discovered at this fracture site.

Cummings et al. (1995) [23] studied risk factors for hip fracture in a cohort of 9,516 women 65 years and over. During a follow-up of 4 years, 192 women experienced their first hip fracture. The relative risk for hip fracture was found to be 1.2 (95% CI: 1.0–1.4) per 190 mg caffeine intake, an estimate that was adjusted for a substantial number of covariates, including BMD.

Meyer et al. (1997) [24] investigated dietary factors (including coffee) and the incidence of hip fractures in an 11-year follow-up of middle-aged (19,752 women and 20,035 men) Norwegians. During follow-up, 213 hip fractures were identified. No linear dose-response relationship was detected but an elevated risk (of borderline significance) for hip fracture restricted to women drinking ≥9 cups (1 cup=115 ml) of coffee daily (RR: 1.94, 95% CI: 0.96–3.91). No interaction was found between intake of calcium and coffee.

In the Iowa Women's Health Study, Hansen et al. (2000) [12] examined the association between caffeine intake and fractures among 34,703 postmenopausal women aged 55–69 years. The total number of fractures at a 6.5-year follow-up was 4,378, including 288 forearm, 1,128 wrist, 275 hip, 416 vertebral and 2,920 other fractures. For the combined fracture sites, the adjusted RR for highest (=≥503.8 mg/day) versus lowest (=0–65.1 mg/day) quintile of caffeine intake was 1.09 (95% CI: 0.99–1.21). Making the same comparisons, wrist fractures were found to be positively (RR: 1.37, 95% CI: 1.11–1.69) and upper arm fractures negatively associated (RR: 0.67, 95% CI: 0.48–0.94) with caffeine intake. No increased risk of hip fracture was detected (RR: 0.92, 95% CI: 0.62–1.36). It should be noted that case ascertainment might have been a problem in this study since it relies largely on self-reports with no X-ray confirmation of the fractures. The participants might have had difficulty to distinguish a forearm from a wrist fracture. Because it is known that osteoporotic fractures are associated with increased mortality [3], the problem with survival bias might also be introduced with the use of self-reports of fractures. Another problem in the study is that it is unclear if all the reported fractures could be classified as osteoporotic.

Conversely, no association between consumption of coffee or caffeine intake and risk of osteoporotic fractures was observed in other cohort studies [10–12] or in several case-control studies [14–20]. Explanations for the negative results might be an overly small study size with few fracture cases [13–16, 18, 19, 37], a relatively low consumption of coffee [11], a narrow exposure range [17], lack of analyses of recent coffee consumption [17] and that consumption of tea and coffee was not considered separately [16, 18]. In addition, the study by Kanis et al. [20] only dealt with data regarding the risk of osteoporotic fractures in men.

Proposed mechanisms

There is some experimental evidence supporting a negative effect of caffeine on bone. Following caffeine administration, teratogenic effects on ossification of the fetus have been observed in some [38, 39], but not all [40, 41] rodent studies. Furthermore, a few studies have indicated that high doses of caffeine can influence bone development in rats postnatally [42, 43]. In addition, administration of coffee or caffeine to rats was followed by a negative calcium balance [44, 45], an effect that could possibly be explained by an increase in the excretion of urinary and faecal calcium [44, 45].

Several human metabolic studies [46–49] have displayed that caffeine exerts a slight negative effect on calcium balance. All these studies demonstrated that caffeine-induced diuresis generates a rapid increase in the loss of calcium via urine. Though this effect was shown to be affected by night-time compensatory renal calcium conservation, the overall result was net increase in renal excretion of calcium [50]. On the other hand, other investigators [8, 51, 52] could not detect any significant increase in calcium excretion after a high caffeine intake. In these latter studies, however, calcium balance was negative, which probably could be explained by a decrease in calcium absorption [53].

Other researchers have suggested that the negative effect of caffeine on BMD may be detected only at low intake levels of calcium. In the cross-sectional study by Barrett-Connor and co-workers [25] an association between consumption of coffee and a decrease in BMD was found, but only when the intake of milk was low, i.e. the negative effect of 2 cups of coffee or more on bone density was offset by just one glass of milk. Furthermore, Harris and Dawson-Hughes [9] demonstrated that postmenopausal women regarded as low consumers of calcium (<744 mg/day) with a high caffeine intake (>450 mg/day) had significantly more bone loss than women consuming less caffeine. Women with higher intake of calcium did not differ in bone loss, regardless of their caffeine consumption. In addition, Rapuri et al. [54] observed that a caffeine intake in amounts exceeding 300 mg/day accelerated bone loss in the spine in elderly postmenopausal women, an observation especially pronounced for those with the tt genetic variant of vitamin D receptor. Our results extend these findings, indicating that dietary calcium intake may also modulate the association between coffee as well as caffeine intake on the risk of fractures.

Tea and the risk of osteoporotic fractures

Few studies have considered the association between consumption of tea and risk of osteoporotic fractures. Two [17, 20] of three [14, 17, 20] case-control studies have, in fact, reported an inverse association with high tea consumption, whereas none of the cohort studies has shown any significant associations [11, 28]. Other studies [26–28] have observed a positive association between BMD in women and tea consumption. Possible explanations for this increase in BMD may be the fluoride, the phytooestrogen or the antioxidant content of tea [27]. In the present study we were not able to detect any association between tea consumption and fracture risk, which might be explained by few high consumers of tea in our cohort. Drinking green tea, especially rich in phytooestrogens and antioxidants, is also uncommon in Sweden.

Advantages and limitation of our study

There are several advantages of our design. In this study we have been able to use data from a large population-based cohort of middle-aged and elderly women. The mean follow-up of 10 years was sufficiently long to detect an adequate number of osteoporotic fractures. The incidence of osteoporotic fractures in our prospective cohort is high and our analyses include a larger number of fractures compared to most earlier investigations. Because of good case ascertainment by use of X-ray diagnosis, we believe that the fractures found in the cohort are well confirmed. All fractures were identified by registers and thus probably only a small proportion of the fractures in the cohort was overlooked. The amount of coffee consumed in this cohort varied considerably. In contrast to investigations carried out in other countries, there are many participants in this study who consume high amounts of coffee. Another advantage of our design is the focus not only on caffeine intake but also on the exposure to coffee and tea separately. This might be an important point because some studies have indicated that tea could have a positive influence on BMD [26–28]. Our estimates were only marginally affected when adjustments were made for several conceivable covariates, e.g. body weight, vitamin A, vitamin D, alcohol and total energy intake. The prospective design with first fractures enabled us to eliminate selective information that was due to recall bias or changes in dietary habits because of the fracture event. Unknown factors may, however, have distorted our findings.

Moreover, our study has several potential limitations. For instance, it is likely that there may be some degree of error in the exposure measurement since it is based on a single FFQ, although according to a long-term stability study [55] the correlations between food group intakes in 1987 (current FFQ) and in 1997 (second FFQ) were found to be significant ($p<0.0001$). As indicated in the dietary assessment the mean reported energy intake is lower than expected for women aged 40–74 years and we estimated the proportion of subjects below a physical activity level (PAL) of 1.35 to 21.5%.

Another limitation is that data on actual intake of caffeine are lacking as no direct measurements of the beverages were made. The measurement error of caffeine is likely to result in an underestimation of the fracture risk. Furthermore, no information regarding supplements containing caffeine was collected even though the use of these types of preparation was probably unusual in Sweden at the time the participants in this study responded to the FFQ or during the follow-up. Supplemental calcium, vitamin D and medications such as oestrogens, which can affect fracture risk, were also missing. However, in an earlier nested case-control study within the same cohort, coffee intake was not related to oestrogen or supplement use [18].

We also lack data on important lifestyle characteristics such as smoking and physical activity. Yet, in this context it should be mentioned that some cohort studies [21–24] have quantified and adjusted for smoking in their coffee and caffeine analyses without any substantial effects on the fracture risk estimates. Thus, it might be questioned if adjustment for smoking would have resulted in a substantial change of our risk estimates. In addition, we did adjust for total energy intake that can be regarded as a proxy variable for physical activity, i.e. individuals with a high-energy intake are more prone to have a higher physical activity [56].

Summary

In summary, our observation demonstrates that Swedish middle-aged and elderly women consuming caffeine in amounts equivalent to approximately 4 cups (600 ml) of coffee or more per day have an increased risk of osteoporotic fractures when their calcium intake was low. This is an important observation in view of the nutritional habits and high risk of fractures of many elderly women.

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