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Short communication
No association between coffee, tea or caffeine consumption and breast cancer risk in a prospective cohort study

Guy Fagherazzi[1,2], Marina S Touillaud[1,2], Marie-Christine Boutron-Ruault[1,2], Françoise Clavel-Chapelon[1,2,*] and Isabelle Romieu[3]

[1]INSERM (Institut National de la Santé et de la Recherche Médicale), Center for Research in Epidemiology and Population Health (CESP), U1018, Institut de cancérologie Gustave-Roussy, 114 rue Edouard Vaillant, F-94805 Villejuif, France: [2]Paris-South University, UMRS 1018, Villejuif, France: [3]National Institute of Public Health, Mexico, DF, Mexico

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Abstract

Objective: Numerous mechanisms for the effects of coffee, tea and caffeine on the risk of breast cancer have been suggested. Caffeine intake has already been associated with high plasma levels of female hormones, but associations have not been clearly demonstrated in epidemiological studies.

Design: We examined prospectively the association of coffee, tea and caffeine consumption with breast cancer risk in a French cohort study.

Setting: Dietary information was obtained from a 208-item diet history questionnaire self-administered in 1993–1995. Multivariable Cox proportional hazards regression models were used to estimate hazards ratios and 95 % confidence intervals.

Subjects: The study was conducted on 67 703 women with available dietary information. During a median follow-up of 11 years, 2868 breast cancer cases were diagnosed.

Results: Median intake was 280 ml/d (2·2 cups/d) for coffee and 214 ml/d (1·7 cups/d) for tea. Median caffeine intake was 164 mg/d. No association was found between consumption of coffee, tea or caffeine and breast cancer risk. Sub-analyses by tumour receptor status, menopausal status, type of coffee (regular or decaffeinated) and meals at which beverages were drunk led to the same conclusion.

Conclusions: Results from this prospective study showed no relationship between coffee, tea or caffeine intake and breast cancer risk overall or by hormone receptor status.

Keywords
Coffee
Tea
Caffeine
Breast cancer risk
Cohort
Cox model

Numerous mechanisms for the effects of coffee, tea and caffeine on the risk of breast cancer have been suggested. For instance, caffeine intake has been associated with high plasma levels of female hormones[1,2]. In epidemiological studies consumption of coffee, tea and caffeine has been hypothesized to either increase or decrease the risk of developing breast cancer[3–9], but associations have not been clearly demonstrated. A recent meta-analysis found no association after summarizing results from cohort and case–control studies[10]. However, two major cohort studies showed a possible increased risk in post-menopausal women who drank more than 4 cups of coffee daily[7] and in women with tumours that were either negative for oestrogen- and progesterone-receptor status or larger than 2 cm[11]. In contrast, a recent review evoked a slight beneficial effect of high consumption of coffee on premenopausal breast cancer risk[12]. This potential relationship remains to be evaluated in a large prospective cohort with detailed dietary information.

Experimental methods

The design of the Etude Epidémiologique auprès des Femmes de la Mutuelle Générale de l'Education Nationale (E3N) cohort has been described previously[13]. Briefly, the cohort is composed of 98 995 women living in France who were between 40 and 65 years of age at the time of recruitment in 1990 and insured by the national health insurance system primarily covering teachers. Demographic, anthropometric, reproductive, lifestyle and medical data were collected in self-administered questionnaires sent at baseline and then biennially for follow-up. Usual diet over the previous year was assessed using a 208-item dietary history questionnaire sent out in 1993, developed and validated for the French population[14]. Portion sizes were estimated using a photo album, also validated[15]; for coffee and tea, six different cup sizes could be selected at each meal (70, 150, 200, 250, 300 or 400 ml) and were then converted into standardized

*Corresponding author: Email clavel@igr.fr

125 ml cups/d for the analysis. Food consumption was converted into nutrient intakes by means of a food composition table derived from the French national food composition table. We estimated the average daily caffeine intake by computing the consumption of all food sources of caffeine and the caffeine content found in the literature for these foods; in our study, the caffeine contents were 72·8 mg/125 ml coffee, 13·8 mg/125 ml tea, 16·1 mg/125 ml chicory beverage, 17·6 mg/330 ml cola, 2·1 mg/30 g chocolate candy and 17·8 mg/30 g plain chocolate.

Women with complete dietary data, with no history of cancer (except for skin basal cell carcinoma, breast lobular carcinoma *in situ* or colorectal cancer *in situ*) and with follow-up after the dietary questionnaire were selected for the present analysis. Women with extreme, physiologically implausible dietary values (i.e. in the bottom or top 1 % of the ratio between energy intake and required energy calculated after taking into account age, weight and height) were excluded, leaving 67 703 women for analysis.

Participants contributed person-years of follow-up starting from the date at which they had completed the dietary questionnaire up to the date of diagnosis of invasive breast cancer as first primary cancer (for cases), date of diagnosis of another cancer, date of the last completed questionnaire or July 2005, whichever came first. Because incident cases of cancer were self-reported by the women in follow-up questionnaires, pathology reports were systematically requested from patients or their doctors to confirm the diagnosis of invasive breast cancer. Histological confirmation was obtained for 96 % of cases.

Statistical analyses

Multivariable Cox proportional hazards regression models were used to estimate hazards ratios (HR) of breast cancer and their 95 % confidence intervals associated with the number of cups (defined as 125 ml) of coffee or tea consumed daily on average compared with none, and for each quartile of caffeine intake compared with the lowest. We also computed coffee, tea and caffeine intake per meal and analysed them separately. Sensitivity analyses were led by type of coffee (regular and decaffeinated). A standard method was used to adjust for energy in every model. Interactions were tested.

Results

Among the 67 703 women included in the present analysis, 2868 cases of invasive breast cancer (634 premenopausal and 2234 postmenopausal) were diagnosed during 707 137 person-years of follow-up between 1993 and 2005 (median duration, 11 years). Coffee was consumed by 85 % (median intake, 280 ml/d, corresponding to 2·2 cups) and tea by 59 % (median intake, 214 ml/d, corresponding to 1·7 cups) of the women. Median caffeine intake (69 % from coffee and tea consumption) was 164 mg/d (range 0·1–724 mg/d) among consumers (85 % of the population). Baseline characteristics of the study population are presented in Table 1. Overall, similar distributions were observed for all the presented characteristics in the different categories of coffee, tea and caffeine consumption.

Coffee and tea consumption was not associated with risk of breast cancer, neither overall or according to menopausal status, oestrogen- or progesterone-receptor status, which was available for 2268 (79 %) cases (Table 2). Nor was caffeine intake related to risk of breast cancer. Results remained similar when considering coffee, tea and caffeine intakes in the same model or when considering different types of coffee (regular or decaffeinated).

When we tested whether coffee, tea and caffeine intakes were differentially associated with breast cancer risk according to the time of day at which beverages were drunk, no differences were observed (data not shown).

Discussion

In the present prospective analysis we found no association between coffee, tea or caffeine consumption and risk of breast cancer, either overall or as defined by hormone receptor status subtype or menopausal status. No association was observed when considering the time of day at which coffee or tea was drunk (during meals) and when considering types of coffee (regular and decaffeinated).

Our results are in accordance with a recent cohort study in the Netherlands[3] and a meta-analysis of nine cohort and nine case–control studies, which showed no association between coffee drinking and breast cancer risk[10]. However, two prospective studies reported an inverse association in specific subgroups. Results from the Nurses' Health Study[7] showed a negative relationship between consumption of caffeine-containing beverages (coffee and tea) and postmenopausal breast cancer risk in women who drank 4 cups (1 cup = 233 ml) or more per day. In the Women's Health Study, an analysis of 38 432 women showed an increased risk of breast cancer associated with caffeine intake for tumours negative for oestrogen- and progesterone-receptor status or larger than 2 cm[11]. A recent review suggested a decrease in premenopausal breast cancer risk associated with drinking at least 4 cups of coffee daily[12]. In our study, we found no association pre- or postmenopause, or according to hormone receptor status. This lack of association in our study might be due to an insufficient variability in daily amount of coffee consumed by the women of the cohort. Michaud *et al.*[16] and Bhoo *et al.*[3] have reported coffee and tea consumptions in some countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC). For coffee, Denmark had the highest coffee consumption (median 900 ml/d) and Italy and Spain had the lowest (90 and 93 ml/d, respectively), whereas the median value in our population was 280 ml/d. However, in Sweden,

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Table 1 Baseline characteristics of the study population: women living in France, aged 40–65 years at recruitment in 1990, E3N cohort (*n* 67 703)

	Coffee (cups/d)								Tea (cups/d)								Caffeine (mg/d)							
	Non-consumers (*n* 9963)		≤1 (*n* 11 905)		1·1–3 (*n* 26 269)		>3 (*n* 19 566)		Non-consumers (*n* 27 631)		≤1 (*n* 15 204)		1·1–3 (*n* 12 001)		>3 (*n* 12 867)		<88 (*n* 16 807)		88–163 (*n* 16 995)		164–262 (*n* 16 891)		>262 (*n* 17 010)	
	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD	Median	SD
Age (years)	51·8	6·8	52·6	6·9	52·0	6·7	50·4	6·2	51·7	6·7	51·8	6·6	51·4	6·6	51·1	6·5	52·4	6·9	52·3	6·8	51·4	6·5	50·2	6·1
Age at menarche (years)	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4	13·0	1·4
Age at first pregnancy (years)	24·0	3·9	24·0	3·9	24·0	3·7	24·0	3·8	24·0	3·7	24·0	3·8	24·0	3·8	24·0	3·8	24·0	3·8	24·0	3·8	24·0	3·7	24·0	3·8
Age at menopause (years)	51·0	3·8	51·0	3·8	51·0	3·7	51·0	3·7	51·0	3·8	51·0	3·7	51·0	3·7	51·0	3·7	51·0	3·8	51·0	3·7	51·0	3·7	51·0	3·7
Number of children	2·0	1·1	2·0	1·2	2·0	1·2	2·0	1·1	2·0	1·2	2·0	1·1	2·0	1·1	2·0	1·1	2·0	1·2	2·0	1·1	2·0	1·1	2·0	1·1
BMI (kg/m^2)	21·9	3·2	22·1	3·2	22·4	3·2	22·6	3·4	22·6	3·4	22·3	3·2	22·2	3·1	22·0	3·0	22·1	3·3	22·3	3·2	22·4	3·2	22·6	3·4
Total energy intake (kcal/d)	2067	580	2085	567	2107	561	2168	593	2094	582	2169	576	2115	564	2095	567	2055	567	2097	559	2128	567	2185	598
Total energy intake (kJ/d)	8648	2427	8724	2372	8816	2347	9071	2481	8761	2435	9075	2410	8849	2360	8765	2372	8598	2372	8774	2339	8904	2372	9142	2502
	%		%		%		%		%		%		%		%		%		%		%		%	
Schooling																								
Undergraduate	14·7		14·7		15·2		15·1		18·5		14·2		13·0		10·6		15·8		15·4		14·4		14·5	
Graduate	69·7		66·2		67·1		67·6		67·6		67·8		68·1		65·9		68·5		66·3		67·6		67·3	
Postgraduate	15·6		19·1		17·7		17·3		13·9		18·0		18·9		23·5		15·7		18·3		18·0		18·2	
Ever use of oral contraceptives																								
No	41·6		42·0		39·2		35·6		42·4		39·3		36·6		33·5		43·7		40·3		37·3		34·7	
Yes	58·4		58·0		60·8		64·4		57·6		60·7		63·4		66·5		56·3		59·7		62·7		65·3	
Current use of hormone replacement therapy																								
No	69·7		67·2		67·8		71·4		70·3		68·5		68·1		67·7		68·4		67·4		68·4		71·8	
Yes	30·3		32·8		32·2		28·6		29·7		31·5		31·9		32·3		31·6		32·6		31·6		28·2	
Personal history of benign breast disease																								
No	70·4		71·8		71·9		71·2		71·9		71·0		71·8		70·7		71·4		71·9		71·4		70·9	
Yes	29·6		28·2		28·1		28·8		28·1		29·0		28·2		29·3		28·6		28·1		28·6		29·1	
History of breast cancer in the family																								
No	88·4		88·0		88·3		88·4		88·6		88·2		88·0		87·9		88·2		88·0		88·5		88·3	
Yes	11·6		12·0		11·7		11·6		11·4		11·8		12·0		12·1		11·8		12·0		11·5		11·7	
Menopausal status																								
Premenopause	42·1		39·2		40·5		47·2		41·5		41·9		42·9		44·7		39·3		39·9		42·6		48·1	
Postmenopause	57·9		60·8		59·5		52·8		58·5		58·1		57·1		55·3		60·7		60·1		57·4		51·9	

Table 2 Multivariable hazards ratios and 95 % confidence intervals* for invasive breast cancer according to coffee and tea consumption and caffeine intake: E3N cohort (*n* 67 703 women), 1993–2005

					Hormone receptor status of the tumour											
		All			ER^+/PR^+			ER^+/PR^-			ER^-/PR^+			ER^-/PR^-		
Beverage	Median daily intake	Cases	HR	95 % CI	Cases	HR	95 % CI	Cases	HR	95 % CI	Cases	HR	95 % CI	Cases	HR	95 % CI
Coffee																
Non-consumers	0	410	1·00	Reference	179	1·00	Reference	65	1·00	Reference	21	1·00	Reference	61	1·00	Reference
≤1 cup†/d	70 ml	491	1·02	0·91, 1·15	233	1·00	0·84, 1·20	78	0·87	0·65, 1·16	19	0·88	0·48, 1·61	51	0·67	0·47, 0·95
1·1–3 cups/d	240 ml	1133	0·98	0·85, 1·11	529	1·04	0·90, 1·21	183	0·94	0·74, 1·20	36	0·74	0·44, 1·25	147	0·87	0·66, 1·15
>3 cups/day	540 ml	834	1·02	0·90, 1·16	379	0·98	0·85, 1·20	156	1·05	0·83, 1·34	24	0·66	0·39, 1·12	105	0·81	0·61, 1·07
P for trend‡			0·79			0·57			0·05			0·10			0·62	
Tea																
Non-consumers	0	1153	1·00	Reference	542	1·00	Reference	197	1·00	Reference	34	1·00	Reference	160	1·00	Reference
≤1 cup†/d	33 ml	652	0·97	0·84, 1·18	275	0·89	0·92, 1·23	115	1·01	0·81, 1·27	29	1·52	0·94, 2·44	78	0·84	0·64, 1·10
1·1–3 cups/d	250 ml	525	1·01	0·89, 1·15	257	1·06	0·92, 1·23	81	0·90	0·70, 1·16	18	1·17	0·67, 2·04	59	0·81	0·60, 1·08
>3 cups/day	586 ml	538	0·79	0·62, 1·01	246	0·93	0·82, 1·06	89	0·87	0·70, 1·09	19	1·10	0·69, 1·79	67	0·78	0·60, 1·01
P for trend‡			0·22			0·19			0·92			0·83			0·63	
Caffeine																
<88 mg/d	48 mg	698	1·00	Reference	320	1·00	Reference	102	1·00	Reference	32	1·00	Reference	91	1·00	Reference
88–163 mg/d	125 mg	722	1·01	0·93, 1·11	335	1·00	0·88, 1·15	129	1·14	0·90, 1·19	27	0·92	0·58, 1·15	84	0·91	0·70, 1·15
164–262 mg/d	207 mg	733	1·04	0·94, 1·15	339	1·03	0·89, 1·19	124	1·15	0·90, 1·19	19	0·60	0·34, 1·19	96	1·04	0·79, 1·19
>262 mg/d	351 mg	715	1·02	0·93, 1·13	326	0·99	0·86, 1·16	127	1·20	0·94, 1·16	22	0·66	0·39, 1·16	93	1·01	0·77, 1·16
P for trend‡			0·36			0·65			0·10			0·15			0·40	

ER^+, positive oestrogen receptor; ER^-, negative oestrogen receptor; PR^+, positive progesterone receptor; PR^-, negative progesterone receptor.
*Multivariable hazards ratios and 95 % confidence intervals calculated by Cox proportional hazards regression models using age as the time scale and adjusted for baseline variables (total energy intake, ever use of oral contraceptives, age at menarche, age at menopause, number of children, age at first pregnancy, history of breast cancer in the family and years of schooling) and time-dependent variables (current use of postmenopausal hormone therapy (for postmenopausal women only), personal history of benign breast disease, menopausal status and BMI).
†1 cup = 125 ml.
‡Test for linear trend using median values in each quartile as an ordinal variable.

where coffee is largely consumed, a cohort study did not find any association regarding breast cancer risk[5]. Women in France consumed more coffee than women in the USA: in 1989, the mean daily consumption of coffee was 1·4 cups (same standardization) daily in US women[17] whereas in our analysis in 1993, women drank a median of 2·2 cups/d. For tea, our population had a median value of 214 ml/d and was among the highest tea consumers in EPIC; only the UK, Denmark and the Netherlands had higher median values (532, 309 and 261 ml/d, respectively)[3,16].

Results in the literature on tea consumption and breast cancer risk are inconsistent. While most cohort studies reported no significant association between overall tea consumption and breast cancer risk[7,18,19], one study suggested that black tea may be positively associated with risk of tumours having positive oestrogen- and progesterone-receptor status[5]. Other case–control studies suggested a negative association for green tea in China[20,21]. In our study in a French population, we found no association between tea consumption and breast cancer risk. Although the type of tea drunk was not available in our data, it is reasonable to assume that it was mostly black tea, traditionally consumed in France.

To explain a potential association between coffee and tea consumption and risk of breast cancer, considered an oestrogen-dependent disease, hypotheses regarding the effects of compounds of the methylxanthine family, including caffeine, have been proposed. Caffeine has been associated with increasing blood levels of oestrone, sex-hormone-binding globulin and decreasing plasma free oestradiol[22], and all of these factors are associated with reduced oestrogenic exposure of breast cells[11]. Moreover, in experimental studies, caffeine was suggested to both stimulate and suppress the development of mammary tumours[23]. Other components of coffee and tea have antioxidant properties (e.g. polyphenols).

Caffeine may differentially affect glucose metabolism as a negative relationship between caffeine intake and glucose absorption, glucose hepatic output and glucose storage has been shown[24,25]. Therefore it might be hypothesized that its effects differ according to the time of day at which the beverage is drunk, thereby potentially affecting breast cancer risk[26]. However, our data did not confirm this hypothesis.

In conclusion, our prospective study showed no association between coffee, tea or caffeine consumption and breast cancer risk.

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