



Coffee and Green Tea Consumption and Subsequent Risk of Malignant Lymphoma and Multiple Myeloma in Japan: The Japan Public Health Center-based Prospective Study

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Abstract

Background: The aim of this study was to investigate the association of coffee and green tea consumption and the risk of malignant lymphoma and multiple myeloma in a large-scale population-based cohort study in Japan.

Methods: In this analysis, a total of 95,807 Japanese subjects (45,937 men and 49,870 women; ages 40–69 years at baseline) of the Japan Public Health Center-based Prospective Study who completed a questionnaire about their coffee and green tea consumption were followed up until December 31, 2012, for an average of 18 years. HRs and 95% confidence intervals were estimated using a Cox regression model adjusted for potential confounders as a measure of association between the risk of malignant lymphoma and multiple myeloma associated with coffee and green tea consumption at baseline.

Results: During the follow-up period, a total of 411 malignant lymphoma cases and 138 multiple myeloma cases were identified. Overall, our findings showed no significant association between coffee or green tea consumption and the risk of malignant lymphoma or multiple myeloma for both sexes.

Conclusions: In this study, we observed no significant association between coffee or green tea consumption and the risk of malignant lymphoma or multiple myeloma.

Impact: Our results do not support an association between coffee or green tea consumption and the risk of malignant lymphoma or multiple myeloma. *Cancer Epidemiol Biomarkers Prev*; 26(8); 1352–6. ©2017 AACR.

Introduction

Several studies suggested that coffee and green tea consumption may decrease the risk of some types of cancers (1, 2). However, epidemiologic evidence for this protective effect on malignant lymphoma and multiple myeloma is scarce. Here, we investigated the association between coffee and green tea consumption and the risk of malignant lymphoma and multiple myeloma in a large-scale population-based cohort study in Japan.

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Materials and Methods

Study population

The details of study design of the Japan Public Health Center-based Prospective Study have been detailed elsewhere (3). Briefly, the study was launched in 1990 for cohort I and in 1993 for cohort II. Cohort I covered five prefectural public health center (PHC) areas (Iwate, Akita, Nagano, Okinawa-Chubu, and Tokyo) and cohort II covered six (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa-Miyako, and Osaka). A baseline self-administered questionnaire survey on various life-style factors, including coffee and green tea consumption, was conducted in 1990 for cohort I and in 1993 to 1994 for cohort II, with a high response rate (81%). In the current analysis, all subjects in one public health center area (Tokyo) were excluded because their incidence data were not available, and some subjects in another area (Suita, Osaka) were also excluded because different definitions of the study population had been applied. We further excluded participants met the following exclusion criteria: (i) non-Japanese nationality; (ii) late report of emigration before the start of the follow-up period; (iii) incorrect birth date; (iv) duplicate registration; (v) later withdrawal of consent; (vi) self-reported history of cancer at baseline survey; (vii) missing values for coffee or green tea consumption. Finally, a total of 95,807 Japanese subjects (45,937 men and 49,870 women; age 40–69 years at baseline) who completed a questionnaire about their coffee and green tea consumption were included in

Table 1. Baseline characteristics of study subjects by coffee and green tea consumption

	Coffee				Green tea				
	Almost none	1-4 times/week	1-2 cups/day	≥3 cups/day	Almost none	1-4 times/week	1-2 cups/day	3-4 cups/day	≥5 cups/day
Men (n = 45,937)									
Person-years	251,251	249,745	204,886	105,546	98,613	113,508	182,614	213,632	203,061
No. of subjects	14,353	13,940	11,614	6,030	5,465	6,326	10,501	12,216	11,429
Proportion (%)	31	30	25	13	12	14	23	27	25
Age (y) ±SD	53.8 ± 7.8	52.2 ± 7.8	51.0 ± 7.9	48.8 ± 7.4	50.7 ± 7.5	49.4 ± 7.3	51.1 ± 8.0	52.6 ± 8.2	54.0 ± 7.7
Body mass index (kg/m ²) ± SD	23.0 ± 2.9	23.1 ± 2.8	23.0 ± 2.8	22.9 ± 3.0	23.4 ± 3.0	23.4 ± 3.0	23.0 ± 2.8	22.8 ± 2.8	22.9 ± 2.8
Smoking status (%)									
Never smoker	28.9	25.5	22.2	13.5	28.3	27.0	24.6	23.6	21.8
Former smoker	27.9	24.8	21.8	15.5	21.8	21.7	23.2	54.9	25.1
Current smoker	43.3	49.8	56.0	71.0	49.9	51.3	52.2	51.5	54.1
Heavy drinker (≥300 ethanol g/wk; %)	29.1	25.4	22.4	19.1	25.9	26.1	25.2	24.4	24.2
Occupation (%)									
Professionals and office workers	15.2	16.9	23.2	26.6	14.9	19.2	22.1	20.5	17.4
Sales clerk or others	19.8	22.2	24.2	28.0	24.2	25.3	23.2	21.8	21.2
Farmers	28.5	26.2	18.8	15.3	22.1	19.3	20.8	23.8	29.2
Manual laborers	16.6	27.8	27.4	25.8	29.9	30.1	27.5	26.2	24.5
Unemployed	8.5	5.9	5.5	3.5	7.4	5.0	5.5	6.7	6.9
Missing	1.4	1.0	0.9	0.9	1.5	1.2	1.0	1.1	0.9
Women (n = 49,870)									
Person-years	309,600	281,705	264,537	84,688	113,144	122,398	190,993	258,122	255,871
No. of subjects	16,541	14,798	13,987	4,544	5,849	6,349	10,140	13,877	13,655
Proportion (%)	33	30	28	9	12	13	20	28	27
Age (y) ±SD	55.2 ± 7.7	52.5 ± 7.8	50.2 ± 7.6	47.7 ± 6.9	50.7 ± 7.4	49.7 ± 7.3	51.3 ± 8.0	53.1 ± 8.2	54.1 ± 7.9
Body mass index (kg/m ²) ± SD	23.2 ± 3.3	23.1 ± 3.1	22.9 ± 3.1	22.7 ± 3.1	23.2 ± 3.3	23.1 ± 3.2	22.9 ± 3.1	22.9 ± 3.1	23.1 ± 3.2
Smoking status (%)									
Never smoker	94.4	94.3	91.7	81.5	90.7	91.9	93.0	93.8	91.5
Former smoker	1.3	1.4	1.5	2.3	2.0	1.5	1.4	1.2	1.6
Current smoker	4.4	4.3	6.9	16.3	7.2	6.6	5.6	5.0	6.9
Heavy drinker (≥300 ethanol g/wk; %)	1.0	1.0	0.8	1.2	1.4	1.7	0.7	0.6	0.9
Occupation (%)									
Professionals and office workers	6.5	9.3	16.0	21.4	9.0	12.5	14.3	11.5	9.3
Sales clerk or others	15.2	17.1	20.8	25.3	19.0	20.8	19.2	17.2	17.2
Farmers	28.4	25.9	16.0	10.9	22.7	17.9	19.9	23.0	26.3
Manual laborers	11.9	13.5	15.5	14.2	15.9	16.2	15.8	12.8	10.4
Unemployed	36.9	33.3	30.8	27.2	31.9	31.2	29.7	34.6	36.0
Missing	1.1	1.0	1.0	1.0	1.4	1.3	1.1	0.9	0.8

this analysis. The study protocol was approved by the institutional review boards of the National Cancer Center, Japan, and Aichi Cancer Center Research Institute.

Outcome

Cancers were identified by active patient notification from major local hospitals in the study area and by data collection from population-based cancer registries with approval. Information on the cause of death was supplemented by checking death certificate files with permission. Malignant lymphoma and multiple myeloma were coded using the International Classification of Diseases for Oncology, Third Edition (4). Malignant lymphoma (morphology code: 959–9729823) and multiple myeloma (9732) were included in the current analysis.

Exposure data

Exposure data are based on a baseline self-administered questionnaire survey about various health habits, including coffee and green tea consumption and other lifestyle factors. Information on coffee and green tea consumption was obtained in terms of the frequency and amount of each beverage consumed according to the following categories: hardly ever, 1–2 d/wk, 3–4 d/wk and almost daily (further divided into 1–2 cups/day, 3–4 cups/day or

5 cups/day). For the current analysis, we further grouped these categories based on their distribution among the subjects (coffee consumption: almost none, 1–4 times/week, 1–2 cups/day, ≥3 cups/day and green tea consumption: almost none, 1–4 times/week, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day).

Statistical analysis

Person-years of follow-up from the date of baseline survey were calculated until the date of diagnosis of malignant lymphoma or multiple myeloma, date of death, move from the PHC area, or December 31, 2012, whichever occurred first. Multivariate-adjusted HRs and 95% confidence intervals (CI) of malignant lymphoma and multiple myeloma were calculated for coffee consumption (almost none, 1–4 times/week, 1–2 cups/day, ≥3 cups/day) and green tea consumption (almost none, 1–4 times/week, 1–2 cups/day, 3–4 cups/day, ≥5 cups/day) at baseline by a Cox proportional hazards model. We also evaluated the *P* value for trend by assignment of ordinal variables in each category. We estimated two types of HR: (i) adjusted for age at baseline (continuous), gender (men or women) and study area (10 PHC areas); and (ii) further adjusted for smoking status (never, former, and current smoker), alcohol consumption (nondrinkers, occasional drinkers, <300

Table 2. HRs and 95% CIs of malignant lymphoma and multiple myeloma according to coffee and green tea consumption

	Coffee				Green tea				<i>P</i> _{trend}	
	Almost none	1-4 times/week	1-2 cups/day	≥3 cups/day	Almost none	1-4 times/week	1-2 cups/day	3-4 cups/day		≥5 cups/day
Malignant lymphoma										
Total										
Person-years	560,851	531,449	469,423	190,233	211,756	235,907	373,607	471,754	458,931	
No. of cases	148	132	92	39	41	37	104	123	106	
HR ^a (95% CI)	1.00 (Reference)	1.06 (0.83-1.34)	0.97 (0.74-1.27)	1.14 (0.79-1.65)	1.00 (Reference)	0.87 (0.55-1.35)	1.35 (0.93-1.96)	1.13 (0.79-1.64)	0.91 (0.63-1.32)	0.522
HR ^b (95% CI)	1.00 (Reference)	1.04 (0.82-1.32)	0.98 (0.75-1.29)	1.16 (0.80-1.69)	1.00 (Reference)	0.84 (0.53-1.31)	1.38 (0.92-1.94)	1.10 (0.76-1.59)	0.89 (0.61-1.29)	0.462
Men										
Person-years	251,251	249,745	204,886	105,546	98,613	113,508	182,614	213,632	203,061	
No. of cases	70	80	57	30	22	20	62	68	65	
HR ^a (95% CI)	1.00 (Reference)	1.25 (0.90-1.72)	1.19 (0.83-1.71)	1.43 (0.92-2.23)	1.00 (Reference)	0.88 (0.48-1.62)	1.52 (0.92-2.50)	1.28 (0.78-2.11)	1.14 (0.69-1.89)	0.599
HR ^b (95% CI)	1.00 (Reference)	1.21 (0.87-1.68)	1.20 (0.83-1.73)	1.45 (0.92-2.30)	1.00 (Reference)	0.81 (0.44-1.50)	1.45 (0.87-2.39)	1.21 (0.73-2.00)	1.08 (0.65-1.79)	0.693
Women										
Person-years	309,600	281,705	264,537	84,688	113,144	122,398	190,993	258,122	255,871	
No. of cases	78	52	35	9	19	17	42	55	41	
HR ^a (95% CI)	1.00 (Reference)	0.88 (0.62-1.25)	0.76 (0.50-1.15)	0.76 (0.37-1.55)	1.00 (Reference)	0.85 (0.44-1.64)	1.17 (0.67-2.03)	0.97 (0.56-1.67)	0.66 (0.38-1.17)	0.107
HR ^b (95% CI)	1.00 (Reference)	0.89 (0.62-1.28)	0.81 (0.53-1.24)	0.82 (0.40-1.68)	1.00 (Reference)	0.87 (0.45-1.69)	1.21 (0.70-2.11)	0.96 (0.56-1.67)	0.67 (0.38-1.19)	0.101
Multiple myeloma										
Total										
Person-years	560,851	531,449	469,423	190,233	211,756	235,907	373,607	471,754	458,931	
No. of cases	52	48	27	11	14	15	24	51	34	
HR ^a (95% CI)	1.00 (Reference)	1.12 (0.76-1.67)	0.85 (0.52-1.38)	0.98 (0.50-1.93)	1.00 (Reference)	0.97 (0.47-2.03)	0.82 (0.42-1.61)	1.18 (0.64-2.19)	0.73 (0.38-1.39)	0.483
HR ^b (95% CI)	1.00 (Reference)	1.10 (0.73-1.63)	0.89 (0.55-1.45)	1.13 (0.57-2.25)	1.00 (Reference)	0.98 (0.47-2.03)	0.84 (0.43-1.66)	1.18 (0.64-2.20)	0.74 (0.38-1.41)	0.500
Men										
Person-years	251,251	249,745	204,886	105,546	98,613	113,508	182,614	213,632	203,061	
No. of cases	22	28	11	5	8	7	12	25	14	
HR ^a (95% CI)	1.00 (Reference)	1.43 (0.82-2.50)	0.81 (0.39-1.70)	0.86 (0.32-2.33)	1.00 (Reference)	0.80 (0.29-2.22)	0.72 (0.29-1.81)	1.10 (0.48-2.53)	0.55 (0.22-1.37)	0.384
HR ^b (95% CI)	1.00 (Reference)	1.36 (0.77-2.42)	0.87 (0.41-1.83)	0.98 (0.36-2.71)	1.00 (Reference)	0.81 (0.29-2.28)	0.77 (0.31-1.94)	1.13 (0.49-2.61)	0.55 (0.22-1.37)	0.371
Women										
Person-years	309,600	281,705	264,537	84,688	113,144	122,398	190,993	258,122	255,871	
No. of cases	30	20	16	6	6	8	12	26	20	
HR ^a (95% CI)	1.00 (Reference)	0.85 (0.47-1.50)	0.85 (0.45-1.63)	1.14 (0.45-2.87)	1.00 (Reference)	1.21 (0.42-3.51)	0.95 (0.35-2.59)	1.28 (0.51-3.23)	0.92 (0.36-2.38)	0.830
HR ^b (95% CI)	1.00 (Reference)	0.83 (0.47-1.48)	0.84 (0.44-1.62)	1.25 (0.49-3.17)	1.00 (Reference)	1.18 (0.41-3.44)	0.93 (0.34-2.55)	1.25 (0.50-3.15)	0.92 (0.36-2.38)	0.847

^aHRs are adjusted for age at baseline (continuous), gender (men or women), and study area (10 PHC areas).

^bHRs are adjusted for age at baseline (continuous), gender (men or women), smoking status (never, former, and current smoker), alcohol consumption (nondrinkers, occasional drinkers, <300 and ≥300 ethanol intake/week), body mass index (<18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m²), occupation (professional or office worker, farmer, manual laborer, unemployed, and missing), and study area (10 PHC areas).

^cHRs are adjusted for age at baseline (continuous), smoking status (never, former, and current smoker), alcohol consumption (nondrinkers, occasional drinkers, <300 and ≥300 ethanol intake/week), body mass index (<18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m²), occupation (professional or office worker, farmer, manual laborer, unemployed, and missing), and study area (10 PHC areas).

ethanol intake/week and ≥ 300 ethanol intake/week), body mass index (<18.5 , $18.5\text{--}24.9$, $25\text{--}29.9$, and ≥ 30 kg/m²), and occupation (professional or office worker, sales clerk or other, farmer, manual laborer, unemployed, and missing). All statistical analyses were done using Stata version 13.1 software (Stata Corp.), with a *P* value <0.05 considered to be statistically significant.

Results

During the follow-up period (average, 18.3 years), a total of 411 malignant lymphoma cases and 138 multiple myeloma cases were identified. Table 1 shows the baseline characteristics of study subjects according to coffee and green tea consumption at baseline. Both men and women with high coffee consumption were more likely to be smokers and tended to be younger than those who hardly drank. On the other hand, both men and women with higher green tea tended to be older.

Table 2 shows the adjusted HRs for malignant lymphoma and multiple myeloma in relation to coffee and green tea consumption. Overall, we observed no significant association between coffee or green tea consumption and the risk of malignant lymphoma for both sexes. Similarly, we observed no significant association with the risk of multiple myeloma for both sexes.

Discussion

In this large Japanese population-based cohort study, we observed no significant association between coffee or green tea consumption and the risk of malignant lymphoma or multiple myeloma.

Consistent with our results, a recent meta-analysis has reported that there was no sufficient evidence to support an association between coffee consumption and the risk of malignant lymphoma, with a pooled relative risk for coffee drinker relative to non/occasional drinker of 1.05 (95% CI, 0.89–1.23; ref. 5). In addition, a few studies investigated the association between coffee consumption and the risk of multiple myeloma, but no study showed a significant association. In contrast, two studies reported that green tea consumption reduced the risk of malignant lymphoma and multiple myeloma. The Ohsaki Study, a population-based cohort study in Japan which involved 41,761 participants and 119 lymphoid neoplasm cases, reported that green tea consumption was inversely associated with the risk of lymphoid neoplasms, including malignant lymphoma and multiple myeloma (≥ 5 cups/day vs. <1 cup/day; HR, 0.52; 95% CI, 0.31–0.87; ref. 6). A case-control study of 220 multiple myeloma cases and 220 controls in Northwest China also reported that green tea was significantly associated with a reduced risk of multiple myeloma (>1 times/month vs. never; OR, 0.38; 95% CI, 0.27–0.53; ref. 7). Inconsistency with our finding might be from modest sample size or retrospective design.

In summary, our results do not support an association between coffee or green tea consumption and the risk of malignant lymphoma or multiple myeloma. Further research is needed to confirm our results.

Disclosure of Potential Conflicts of Interest

M. Inoue is the beneficiary of a financial contribution from the AXA Research fund as chair holder of the AXA Department of Health and Human Security,

Graduate School of Medicine, The University of Tokyo. No potential conflicts of interest were disclosed by the other authors.

Disclaimer

The AXA Research Fund had no role in the design of the study, data collection, analysis, interpretation, or manuscript drafting, or in the decision to submit the manuscript for publication.

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