Null Results in Brief

Coffee Consumption Is Not Associated with Ovarian Cancer Incidence

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Introduction

Coffee contains many substances that could conceivably influence the risk of ovarian cancer. In a meta-analysis of the crude data of seven case-control studies of coffee consumption and ovarian cancer published before 1990, the combined odds ratio was 1.3 [95% confidence interval (95% CI), 1.1-1.5] for coffee users versus nonusers (1). Since then, at least six case-control studies have reported on the association of coffee consumption with ovarian cancer risk. Of these, two studies found a statistically significant increased risk of ovarian cancer associated with coffee consumption (2, 3), one study found a statistically significant inverse association (4), and three studies did not show any significant association (5-7).

To date, only two cohort studies, both with a small number of cases, have examined the relation between coffee consumption (assessed at baseline) and ovarian cancer risk. Although coffee consumption was not associated with mortality from ovarian cancer (n = 50 cases) in a cohort of Seventh-day Adventists (8), a Norwegian cohort reported a positive, but statistically nonsignificant, association between coffee consumption and ovarian cancer incidence (n = 93 cases; ref. 9). Given the inconclusive results on coffee consumption and ovarian cancer risk, we sought to prospectively evaluate long-term coffee consumption, using repeated measures of diet, in relation to incidence of invasive epithelial ovarian cancer among 61,057 women in the Swedish Mammography Cohort.

Materials and Methods

The population-based Swedish Mammography Cohort comprises 66,651 women from two counties in central Sweden who were 40 to 76 years of age on enrollment between 1987 and 1990 (10). The Swedish Mammography Cohort has been approved by the Ethics Committees at the Karolinska Institutet (Stockholm) and the Uppsala University Hospital. Dietary intake data were collected at baseline and in 1997 by self-administered food-frequency questionnaires. The Spearman correlation coefficient between coffee consumption and ovarian cancer risk, as assessed by the baseline questionnaire compared with the mean of four 1-week weighed diet records, was 0.63.

The study population for the present analysis consisted of 61,057 who were cancer-free and had at least one ovary at recruitment and who had a total energy intake within 3 SDs from the $\log_e$-transformed mean energy intake in the cohort. Complete follow-up of the cohort was accomplished through linkages with the Swedish Population, Death, Cancer, and In-Patient registers. Each participant accrued follow-up time from the date of entry into the cohort to the date of ovarian cancer diagnosis, death, bilateral oophorectomy, migration, or December 31, 2004, whichever occurred first.

To better represent long-term coffee consumption and to reduce random within-person variation, dietary information from the baseline questionnaire was used to predict ovarian cancer incidence from baseline through 1997, and the average of the baseline and 1997 intake was used to predict ovarian cancer incidence from 1998 through December 2004. Rate ratios (RR) with 95% CIs were estimated using Cox proportional hazards models stratified on age in months and the year of enrollment. Multivariate models adjusted for age, body mass index, education, parity, oral contraceptive use, and intakes of total energy, fruit, vegetables, milk, and tea. We conducted tests for linear trend by assigning the median value to each category of coffee consumption and treating this variable as a single continuous variable. All P values are two sided.

Results

At baseline, 95% of the women reported drinking coffee at least once per month. The mean coffee consumption among drinkers was 2.5 cups per day. Compared with women with low coffee consumption, those with higher consumption were younger, less likely to have a post-secondary education, and consumed more milk but less tea (Table 1).

Table 1. Age-standardized baseline characteristics according to coffee consumption among participants of the Swedish Mammography Cohort

Characteristic	Coffee consumption (cups/d)			
	<1	1	2-3	≥4
Median consumption	0.1	1.0	2.5	4.0
Mean age (y)	54.0	56.6	54.2	49.8
Mean body mass index (kg/m^2)	24.8	24.7	24.7	24.9
Post-secondary education (%)	15	14	13	12
Mean number of child births	2.1	2.1	2.1	2.2
Oral contraceptive use (%)	53	54	54	55
Mean consumption				
Fruits (servings/d)	1.5	1.5	1.5	1.5
Vegetables (servings/d)	1.8	1.8	1.8	1.8
Milk (servings/d)	1.0	1.1	1.2	1.3
Tea (cups/d)	1.1	0.8	0.5	0.3

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Table 2. RRs of invasive epithelial ovarian cancer according to baseline and long-term coffee consumption in the Swedish Mammography Cohort

	Coffee consumption (cups/d)					
	<1	1	2-3	≥4	*P* for trend*	One cup of coffee per day
Baseline intake						
No. cases	26	47	176	52		301
No. person-years of follow-up	82,053	121,086	548,798	168,470		920,407
Age-adjusted RR (95% CI)	1.00	1.11 (0.68-1.81)	0.99 (0.65-1.51)	1.09 (0.67-1.77)	0.97	1.01 (0.90-1.12)
Multivariate RR (95% CI)†	1.00	1.08 (0.66-1.73)	0.96 (0.62-1.47)	1.02 (0.62-1.69)	0.84	0.99 (0.88-1.11)
Long-term intake						
No. cases	24	51	177	49		301
Age-adjusted RR (95% CI)	1.00	1.16 (0.71-1.89)	0.99 (0.65-1.53)	1.12 (0.68-1.84)	0.98	0.98 (0.88-1.08)
Multivariate RR (95% CI)†	1.00	1.13 (0.69-1.86)	0.97 (0.62-1.51)	1.07 (0.64-1.79)	0.85	0.98 (0.88-1.09)

*P for trend calculated by using the median value of each category of coffee consumption as a single continuous variable.
†Multivariate RRs are adjusted for age in months (continuous), body mass index (quartiles), education (less than high school, high school, university), parity (nulliparous, 1-2 children, ≥3 children), oral contraceptive use (ever, never), and intakes of total energy (continuous), fruit (quartiles), vegetables (quartiles), milk (quartiles), and tea (<1 cup/mo, 1 cup/mo to <1 cup/d, 1 cup/d, and ≥2 cups/d).

During 920,407 person-years of follow-up (mean, 15.1 years), 301 women were diagnosed with invasive epithelial ovarian cancer (including 135 of the serous subtype). We observed no association between baseline or long-term coffee consumption and risk of ovarian cancer after adjustment for age only or in multivariate models (Table 2). Coffee consumption was also not associated with risk of serous ovarian cancer (multivariate RR for ≥4 cups/d versus <1 cup/d, 1.11; 95% CI, 0.52-2.35).

Discussion

In this large population-based prospective cohort study, we observed no indication that long-term coffee consumption is associated with incidence of ovarian cancer. Only one previous cohort study has reported on coffee consumption and ovarian cancer incidence. In that cohort, with 93 ovarian cancer cases diagnosed among 21,238 Norwegian women followed for 10 years (9), high coffee consumption was associated with a nonsignificant increased risk of ovarian cancer. However, when examining the RRs across categories of coffee consumption, there was no monotonic dose-response relation (9); compared with the lowest category of coffee consumption (≤2 cups/d), the RRs for increasing categories (3-4, 5-6, and ≥7 cups/d) were 2.3, 2.7, and 2.0. These uncertain estimates may reflect the limited number of cases, especially in the lowest category (n = 5 cases).

Data collected in any observational study are measured with error, and nondifferential measurement error has to be considered as a possible explanation for the lack of association between coffee consumption and ovarian cancer risk in our study. Misclassification of coffee consumption may have attenuated the findings to some degree; however, this is an unlikely explanation for the absence of association over extreme categories of consumption because it is improbable that participants were misclassified from one extreme category to the other. We updated the information about diet during follow-up to provide a better measure of long-term coffee consumption and to reduce random within-person measurement error.

The strengths of our study include a population-based and prospective design, repeated measures of diet, a large size, and a large number of ovarian cancer cases. The prospective nature of the study design precluded recall and selection biases, which may have limited previous case-control studies. The practically complete cohort follow-up minimized the concern that our results have been affected by differential follow-up. Furthermore, our findings are unlikely to be explained by residual confounding because the RR estimates did not appreciably change after simultaneous controlling for potential confounding variables. Nevertheless, the possibility of confounding by unaccounted risk factors cannot be ruled out.

In summary, findings from this large population-based prospective cohort study suggest that consumption of coffee is unlikely to substantially influence the risk of ovarian cancer in middle-aged and older women.

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