



Associations of coffee, tea and caffeine intake with risk of breast, endometrial and ovarian cancer among Canadian women

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ABSTRACT

Background: Although, biologically plausible evidence has implicated coffee, tea and caffeine with carcinogenesis, there is a paucity of data on their associations with risk of cancer among Canadian women. Hence, we assessed their associations with risk of breast, endometrial and ovarian cancers within this population.

Methods: The study comprised a subcohort of 3185 women from a cohort of 39,532 female participants who completed self-administered lifestyle and dietary questionnaires at enrollment. During a median follow-up of approximately 12.2 years, we ascertained 922, 180 and 104 breast, endometrial and ovarian cancer cases, respectively. We used Cox proportional hazards regression models modified for the case-cohort design to estimate the hazard ratios (HR) and 95% confidence intervals (CI) for the associations of coffee, tea and caffeine with risk of selected cancers.

Results: Coffee, tea, and caffeine intake were not associated with overall risk of breast and ovarian cancers. There was, however, a tendency towards an increased risk of breast cancer with increasing levels of total coffee, caffeinated coffee and/or caffeine among premenopausal and normal weight women. Total coffee, caffeinated coffee, and caffeine were inversely associated with risk of endometrial cancer (HR_{per cup increase}: 0.88; 95% CI: 0.79-0.95, HR_{per cup increase}: 0.88; 95% CI: 0.80-0.96 and HR_{per 100mg increase}: 0.93; 95% CI: 0.87-0.99, respectively).

Conclusion: Our findings suggest that coffee and/or caffeine may be associated with reduced risk of endometrial cancer but, probably, associated increased with risk of breast cancer among premenopausal or normal weight women. However, further studies are needed to confirm our findings.

1. Introduction

Coffee and tea are postulated to influence the development of cancer [1–3], but the underlying mechanisms remain unclear. Nevertheless, these beverages contain certain compounds, such as polyphenols and caffeine, which may prevent carcinogenesis through several mechanisms including scavenging free radicals, inhibiting inflammatory processes, minimizing DNA damage, improving insulin sensitivity, increasing levels of sex hormone binding globulin, reducing levels of free estradiol and reducing circulating glucose levels [1,4–9]. Conversely, evidence from some studies has indicated that these beverages may induce carcinogenesis through processes such as tumor cell proliferation [10–13].

Based on these observations, several epidemiological studies have been conducted to elucidate the role that coffee and tea, as well as

caffeine, a component of these beverages, may play in the development of breast, endometrial, and ovarian cancers. While most studies do not support an association of coffee and caffeine intake with risk of breast cancer [14–19], a few studies have shown an inverse association with total coffee intake [20,21]. There is also little support for an association between coffee or caffeine intake and risk of ovarian cancer [13,18,22–24]. More consistent findings have been observed for the association between coffee consumption and risk of endometrial cancer, with most studies reporting an inverse association [7,25–30]. Caffeine, however, does not appear to be associated with risk of endometrial cancer, as the results of epidemiological studies, to date, have mostly been null [28,29,31,32]. Studies assessing overall tea intake have largely failed to observe associations with risk of breast, endometrial or ovarian cancer [23,29,31–35].

Coffee, particularly regular brewed coffee, and tea are among

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Table 1
Characteristics of study population among women from the Canadian Study of Diet, Lifestyle, and Health.

Characteristic	Breast cancer		Endometrial cancer		Ovarian cancer	
	Subcohort (N = 3120)	Cases (N = 922)	Subcohort (N = 2608)	Cases (N = 180)	Subcohort (N = 2826)	Cases (N = 104)
Age at entry (yrs; Median (IQR))	59 (48-71)	51 (44-63)	58 (47-71)	55 (48-66)	58 (48-70)	55 (44-65)
Education (N (%))						
Post-Secondary/Some College or less	1895 (60.7)	541 (58.7)	1570 (60.2)	101 (56.1)	1709 (60.5)	59 (56.7)
Graduate School	1225 (39.3)	381 (41.3)	1038 (39.8)	79 (43.9)	1117 (39.5)	45 (43.3)
Total energy intake (kcal/d; Median (IQR))	2157.1 (1763.3-2157.1)	2136.7 (1776.8-2552.4)	2149.0 (1754.2-2625.3)	2118.9 (1758.2-2537.6)	2153.1 (1760.0-2637.1)	2086.0 (1625.5-2504.6)
Age at menarche (yrs; Median (IQR))	13 (12-13)	13 (12-13)	13 (12-14)	12 (11-13)	13 (12-14)	13 (12-13)
Parity (Median (IQR))	2 (0-3)	2 (0-3)	2 (0-3)	2 (0-3)	2 (0-3)	1 (0-2)
Breast-fed (N (%))	1901 (60.9)	574 (62.3)	1616 (62.0)	105 (58.3)	1752 (62.0)	50 (48.1)
Menopausal status (N (%))						
Premenopausal	1085 (34.8)	500 (54.2)	1076 (41.3)	92 (51.1)	1078 (38.1)	49 (47.1)
Postmenopausal	2035 (65.2)	422 (45.8)	1532 (58.7)	88 (48.9)	1748 (61.9)	55 (52.9)
Oral contraceptive ever (N (%))	1807 (57.9)	652 (70.7)	1540 (59.1)	114 (63.3)	1686 (59.7)	63 (60.6)
HRT ever (N (%))	1070 (34.3)	270 (29.3)	717 (27.5)	59 (32.8)	846 (29.9)	40 (38.5)
Alcohol (g/d; Median (IQR))	4.0 (1.0-14.1)	4.0 (1.0-14.1)	3.0 (0.0-13.1)	4.0 (0-9.6)	4.0 (1.0-13.1)	4.0 (1.0-14.1)
Family history of breast cancer in first degree relative (N (%))	341 (10.1)	122 (13.2)	263 (10.1)	18 (10.0)	285 (10.1)	11 (10.6)
Physical activity (Mets/hr wk; Median (IQR))	13.5 (3.9-27.0)	13.1 (5.7-25.8)	13.9 (4.2-27.5)	11.2 (5.7-25.7)	14.1 (4.2-27.4)	12.4 (4.8-25.1)
BMI (kg/m ² ; Median (IQR))	23.7 (21.5-26.3)	23.7 (21.6-26.5)	23.5 (21.5-26.3)	25.4 (23.5-30.3)	23.6 (21.5-26.3)	23.6 (21.5-26.9)
Pack years of smoking (Median (IQR))	0.0 (0.0-11.3)	0.0 (0.0-14.5)	0.0 (0.0-14.5)	0.0 (0.0-8.5)	0.0 (0.0-14.5)	0.6 (0.0-31.3)
Follow-up time (yrs.; Median (IQR))	13.3 (10.3-15.7)	7.0 (3.9-10.6)	15.1 (10.7-15.7)	8.0 (4.7-10.7)	15.1 (10.7-15.7)	7.5 (3.6-10.5)

commonly consumed beverages in Canada [36]. Despite the existence of biologically plausible evidence suggesting that these beverages, as well as caffeine, may influence a woman's risk of cancer, very few studies have been conducted to assess their role in the development of cancers among Canadian women [13,37]. Thus, in this study we examined the association between coffee, tea and caffeine intake and risk of cancers of the breast, endometrium, and ovary among women in the Canadian Study of Diet, Lifestyle, and Health (CSDLH).

2. Materials and methods

2.1. Study population

A detailed description of the CSDLH was published previously [38]. The CSDLH is a prospective study comprising 73,909 Canadian participants (34,291 males and 39,618 females) who were recruited predominantly from alumni of the Universities of Alberta, Toronto and Western Ontario between 1995 and 1998. A small contingent was also recruited through the Canadian Cancer Society, mostly in 1992 [38].

2.2. Exposure assessment

Information on sociodemographic characteristics, personal medical history, history of cigarette smoking, physical activity, height and weight, menstrual and reproductive history, and use of oral contraceptives and hormone replacement therapy was collected at baseline using a detailed self-administered lifestyle questionnaire. Participants were also provided with tape measures and instructions on how to measure their waist and hip circumferences.

Information on intake of coffee, tea and other caffeine-containing beverages was collected at enrolment into the study as part of a 166-item quantitative food frequency questionnaire (FFQ). This FFQ was calibrated over a 1-year period via a self-administered baseline FFQ, three 24-h diet recalls administered by telephone, and a second FFQ

self-administered one year after the initial FFQ, and was shown to be relatively reliable in determining dietary intake (median correlation coefficients for selected nutrients in women: 0.63, $P < 0.001$, based on the two FFQs) [39]. Each participant was asked to report her usual intake of coffee and tea as never or number of 8 ounce cups consumed daily, weekly or monthly. The caffeine content (mg/day) for caffeine-containing foods was calculated using the Canadian Nutrient File (CNF – 1997 version) [39]. Total caffeine intake was estimated as the sum of the reported amounts of caffeine in coffee, tea, hot chocolate/cocoa, cola (Coca-Cola, Pepsi, other), diet/light pudding, chocolate syrup, strawberry syrup, chocolate spreads, and chocolate bars/candy consumed.

2.3. Cohort follow-up

Participants were followed from enrolment until December 31st, 2010 for those who were resident in Ontario and through December 31st, 2005 for those residing in all other provinces of Canada.

Information on migration out of Canada was not collected as out-migration was very low during the recruitment period for this study (estimated to be less than 0.005%) [40]. Deaths from all causes were ascertained by means of record linkage to the National Mortality Database.

2.4. Outcome and death ascertainment

The outcomes of interest were incident primary breast, endometrial and ovarian cancers. Breast cancer was defined using ICD-9 code 174.0–174.9 and ICD-10 code C50; endometrial cancer was defined using ICD-9 code 182.0–182.9 and ICD-10 code C54.0 while ovarian cancer was defined using ICD-9 code 183.0–183.9 and ICD-10 code C56.0. Incident cancer cases were ascertained via record linkage to the Canadian Cancer Registry (CCR) and to the Ontario Cancer Registry. The CCR is a collaborative effort between the thirteen Canadian

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