Consumption of black tea or coffee and risk of ovarian cancer

J.A. BAKER*, K. BOAKYE†, S.E. McCANN*, G.P. BEEHLER*, K.J. RODABAUGH‡, J.A. VILLELLA‡ & K.B. MOYSICH*

**Department of Epidemiology, Roswell Park Cancer Institute, Buffalo, New York; †Ross University School of Medicine, Edison, New Jersey; and ‡Department of Gynecologic Oncology, Roswell Park Cancer Institute, Buffalo, New York*

Abstract. Baker JA, Boakye K, McCann SE, Beehler GP, Rodabaugh KJ, Villella JA, Moysich KB. Consumption of black tea or coffee and risk of ovarian cancer. *Int J Gynecol Cancer* 2006.

The goal of this study was to investigate the associations between ovarian cancer risk and usual consumption of black tea, regular coffee, or decaffeinated coffee. Using a hospital-based case–control design, participants included 414 women with primary epithelial ovarian, fallopian, or peritoneal cancer and 868 age- and region-matched women with nonneoplastic conditions. All participants completed a comprehensive epidemiologic questionnaire. Black tea consumption was associated with a linear decline in ovarian cancer risk (*P* for trend 0.03), with individuals consuming two or more cups daily experiencing a 30% decline in risk (adjusted OR 0.70, 95% CI 0.51–0.97). Similar declines were noted among individuals consuming two or more cups of decaffeinated coffee daily (adjusted OR 0.71, 95% CI 0.51–0.99; *P* for trend 0.002). However, no association was noted between any level of regular coffee consumption and risk of ovarian cancer. The chemoprotective effects of phytochemicals in black tea and decaffeinated coffee may be important, although the effects of phytochemicals in regular coffee may be counteracted by the elevated risk associated with its higher caffeine content.

KEYWORDS: caffeine, coffee, epidemiologic studies, ovarian neoplasms, tea.

Coffee and tea are readily available and widely consumed beverages containing complex mixtures of biochemically active components that have been hypothesized to influence cancer risk. Both coffee and tea are significant sources of polyphenols, such as phytoestrogens, flavonoids, and catechins[1,2], which have been shown to play a role in a variety of anticarcinogenic processes[1]. In a recent review, tea consumption has also been found to reduce the risk of several other health endpoints, including cardiovascular disease[2]. In contrast to tea, early studies of caffeine and coffee exposure suggested increased cancer risk at several sites[3–6]. More recently, however, coffee has been hypothesized to work indirectly and may modify the effect of other exposures, including polyphenols[7].

Previous studies have suggested that coffee consumption may increase ovarian cancer risk[8–14], although several studies found no association[15–20], and one reported a protective effect[21]. In contrast, results from studies examining consumption of either black tea or decaffeinated coffee have been mixed, with some suggesting a potential protective effect of one or both beverages[11,14,20,22], while others identified no association[15,21,23]. However, many of these studies were limited by small samples[8–12,14,15,17–19,22], and only three examined whether effects differed by histologic subtype of ovarian cancer[13,14,21]. Given these limitations and the inconclusive results of previous studies, we examined usual consumption of black tea, regular coffee, and decaffeinated coffee among ovarian cancer patients and hospital-based controls treated over the course of 16 years at Roswell Park Cancer Institute (RPCI).

Materials and methods

The study population included individuals who received medical care at RPCI in Buffalo, New York, between 1982 and 1998, and who agreed to complete

Address correspondence and reprint requests to: Kirsten B. Moysich, MS, PhD, Department of Epidemiology, A-316 Carlton House, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. Email: kirsten.moysich@roswellpark.org

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a comprehensive epidemiologic questionnaire and an informed consent form approved by the hospital's Institutional Review Board. Individuals without complete information on coffee and tea consumption were excluded. Cases comprised 414 newly diagnosed women with primary epithelial ovarian, fallopian, or peritoneal cancer identified from the RPCI Tumor Registry and Diagnostic Index. Median time between diagnosis and participation was 21 days; 68% of cases participated within 2 months of diagnosis. Controls included 868 women randomly selected from a pool of 5650 eligible women who had received medical services at RPCI for nonneoplastic conditions. These participants came to RPCI with a suspicion of neoplastic disease but were not diagnosed with either benign or malignant conditions. Selected controls were most frequently treated for breast disorders (27%), genitourinary disorders (19%), gastrointestinal disorders (10%), skin disorders (6%), and circulatory disorders (5%). Controls were frequency matched 2:1 to cases on geographic region (inside or outside western New York) and 5-year age intervals.

All participants completed the Patient Epidemiology Data System (PEDS) questionnaire, which is offered to all new patients as part of the admission process and is returned by approximately 50% of patients. The 16-page instrument covers information on tobacco and alcohol consumption, family history of cancer, occupational and environmental exposures, reproductive and medical histories, medication and vitamin usage, and diet. Diet was assessed using a 44-item food frequency questionnaire that assessed usual intake during "the past few years before the current illness." The separate section on beverage intake assessed usual daily servings of black tea, decaffeinated tea, regular coffee, and decaffeinated coffee. Beverage intake was categorized based on the distribution of intake among the controls, with an emphasis on creating meaningful categories. Regular coffee intake was classified as none, $\leq$1 cup/day, 2–3 cups/day, or 4 or more cups/day. Decaffeinated coffee intake was classified as none, $\leq$1 cup/day, or 2 or more cups/day. Black tea intake was classified as none, $<$1 cup/day, 1 cup/day, or 2 or more cups/day. During the period covering data collection (1982–1998), intake of decaffeinated tea, green tea, and herbal teas were uncommon, preventing examination in this study.

Risk of ovarian cancer was estimated using unconditional logistic regression, adjusting for matching variables and identified confounders that changed the odds ratio in any exposure stratum by at least 10%. Confounders were evaluated separately for models examining regular coffee, decaffeinated coffee, and black tea. For all analyses, nondrinkers of the beverage were used as the referent group. *P* for trend was determined by evaluating the significance of the continuous exposure variable in the logistic regression model.

Results

Descriptive characteristics of the study population are shown in Table 1. Due to matching procedures, there were no differences between cases and controls with respect to age or region of residence. Women with ovarian cancer were significantly less likely to report their race as non-Hispanic white, and were less likely to have ever been pregnant, had a live birth, or used hormone replacement therapy. On average, individuals with ovarian cancer sought care at the hospital and participated in the survey 2 years later than participants with nonneoplastic conditions. Women diagnosed with ovarian cancer also reported a shorter

Table 1. Characteristics of 414 ovarian cancer cases and 828 noncancer hospital controls—RPCI, 1982–1998

Characteristic	Cases, *n* (%)	Controls, *n* (%)	P^a
Non-Hispanic white race	391 (94.4)	808 (97.6)	0.004
Currently married	276 (67.3)	515 (62.5)	0.10
High school graduate	340 (83.1)	660 (80.1)	0.20
Yearly income >$25,000	143 (35.7)	246 (30.1)	0.05
First-degree relative with ovarian cancer	19 (4.6)	24 (2.9)	0.12
Ever pregnant	328 (79.4)	714 (86.4)	0.001
Ever live birth	312 (76.5)	686 (83.8)	0.002
Menses were usually irregular	55 (13.3)	134 (16.5)	0.14
Ever took hormone replacement therapy	86 (21.2)	208 (25.9)	0.07
Ever had tubal ligation	49 (12.2)	121 (15.0)	0.19
	Mean (SD)	Mean (SD)	P^b
Age	55.6 (13.7)	55.4 (13.7)	0.85
Year completed questionnaire	1989 (4.6)	1987 (4.0)	<0.001
Usual body mass index (kg/m^2)	26.0 (6.0)	25.3 (5.3)	0.05
Age at onset of menses	12.9 (1.4)	12.8 (1.6)	0.32
Lifetime duration of breastfeeding (months)	3.9 (9.5)	5.8 (12.2)	0.004
Number of live born children	2.2 (1.8)	2.6 (2.0)	<0.001
Years of oral contraceptive use	3.6 (4.3)	3.9 (4.7)	0.42

SD, standard deviation.
[a]Statistical significance tested using Chi-square or Fisher exact test, as appropriate.
[b]Statistical significance tested using two-tailed Student's *t*-test.

lifetime history of breastfeeding and fewer live born children. Cases and controls did not differ with respect to oral contraceptive use.

As shown in Table 2, a linear decline in ovarian cancer risk was noted with increasing black tea consumption (*P* for trend 0.03). Compared to women who did not consume black tea, women with a usual consumption of at least 2 cups/day experienced a 30% decline in ovarian cancer risk (adjusted OR 0.70, 95% CI 0.51–0.97). A similar decline was noted for women who consumed at least two cups of decaffeinated coffee daily (adjusted OR 0.71, 95% CI 0.51–0.99; *P* for trend 0.002). In contrast, no clear association was noted between consumption of regular coffee and ovarian cancer risk. Results did not differ when models were mutually adjusted for consumption of other beverages under investigation (data not shown). In addition, no differences were noted when participants were stratified on menopausal status, body mass index, hormone replacement therapy use, or monthly fruit and vegetable intake (data not shown), which were hypothesized as potential effect modifiers.

Table 3 displays adjusted associations between beverage intake and ovarian cancer risk by histologic subtype. Although cell sizes decrease, resulting in less stable point estimates, results do not appear different for most subtypes of ovarian cancer. A few noteworthy exceptions include a potential increase in the risk of mucinous tumors with all levels of regular coffee consumption and the absence of a protective effect for either tea or decaffeinated coffee with clear-cell tumors.

Discussion

Coffee and tea contain significant amounts of phytochemicals that could potentially affect cancer etiology. Consistent with experimental data suggesting that higher consumption of tea and other polyphenol-containing beverages could reduce cancer risk[1], we observed a 30% decrease in ovarian cancer risk with the highest consumption of either black tea or decaffeinated coffee. Although regular coffee also contains polyphenols, no association was noted between regular coffee intake and ovarian cancer risk, possibly due to regular coffee's higher caffeine content. There are several reasons why the higher doses of caffeine in coffee may explain the absence of a protective effect against ovarian cancer. Caffeine has been shown to reduce the beneficial antioxidant effects of flavonoids[7]. Caffeine consumption may also regulate the cell cycle checkpoint function involved in DNA repair[24], by inhibiting cell proliferation in early stages of the cell cycle[25] and revoking checkpoint responses in later phases[26]. Additionally, caffeine is a known inhibitor of ataxia telangiectasia mutated kinase, the enzyme responsible for phosphorylating and activating p53, thus inhibiting p53-related apoptosis[27].

Table 2. Crude and adjusted risk of ovarian cancer by black tea, regular coffee, and decaffeinated coffee consumption—RPCI, 1982–1998

	Cases, *n* (%)	Controls, *n* (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Black tea consumption[a]				
None	136 (32.9)	229 (27.7)	1.00	1.00
<1 cup/day	118 (28.5)	227 (27.4)	0.88 (0.64–1.19)	0.87 (0.64–1.19)
1 cup/day	66 (15.9)	147 (17.8)	0.76 (0.53–1.08)	0.75 (0.52–1.08)
2 or more cups/day	94 (22.7)	225 (27.2)	0.70 (0.51–0.97)	0.70 (0.51–0.97)
P for trend			0.03	0.03
Regular coffee consumption[b]				
None	139 (33.6)	275 (33.2)	1.00	1.00
≤1 cup/day	107 (25.8)	196 (23.7)	1.08 (0.79–1.48)	1.15 (0.83–1.59)
2–3 cups/day	102 (24.6)	213 (25.7)	0.95 (0.69–1.29)	1.02 (0.74–1.41)
4 or more cups/day	66 (15.9)	144 (17.4)	0.91 (0.64–1.29)	1.05 (0.73–1.52)
P for trend			0.22	0.60
Decaffeinated coffee consumption				
None	228 (57.0)	420 (52.0)	1.00	1.00
≤1 cup/day	101 (25.3)	194 (24.0)	0.96 (0.72–1.28)	1.07 (0.79–1.45)
2 or more cups/day	71 (17.8)	193 (23.9)	0.68 (0.49–0.93)	0.71 (0.51–0.99)
P for trend			0.001	0.002

OR, odds ratio; CI, confidence interval.
[a]Adjusted for age and residence.
[b]Adjusted for age, residence, and year of participation.

Table 3. Adjusted risk of ovarian cancer, by histologic subtype[a], and consumption of black tea, regular coffee, or decaffeinated coffee—RPCI, 1982–1998

	All ($n = 414$) OR (95% CI)	Serous ($n = 255$) OR (95% CI)	Mucinous ($n = 33$) OR (95% CI)	Endometrioid ($n = 49$) OR (95% CI)	Clear cell ($n = 28$) OR (95% CI)	Borderline ($n = 27$) OR (95% CI)
Black tea consumption[b]						
None	1.00	1.00	1.00	1.00	1.00	1.00
<1 cup/day	0.87 (0.64–1.19)	0.94 (0.65–1.36)	0.62 (0.25–1.52)	0.73 (0.35–1.53)	1.16 (0.41–3.26)	0.68 (0.27–1.69)
1 cup/day	0.75 (0.52–1.08)	0.81 (0.53–1.25)	0.12 (0.02–0.94)	0.78 (0.34–1.79)	1.23 (0.40–3.76)	0.49 (0.15–1.54)
2 or more cups/day	0.70 (0.51–0.97)	0.78 (0.53–1.15)	0.75 (0.33–1.74)	0.51 (0.22–1.16)	1.03 (0.35–2.98)	0.16 (0.04–0.73)
Regular coffee consumption[c]						
None	1.00	1.00	1.00	1.00	1.00	1.00
≤1 cup/day	1.15 (0.83–1.59)	1.16 (0.79–1.68)	2.47 (0.90–6.80)	0.77 (0.34–1.78)	1.22 (0.46–3.25)	1.11 (0.34–3.64)
2–3 cups/day	1.02 (0.74–1.41)	0.86 (0.58–1.27)	2.17 (0.77–6.10)	1.05 (0.49–2.22)	0.45 (0.12–1.69)	2.22 (0.81–6.08)
4 or more cups/day	1.05 (0.73–1.52)	0.80 (0.51–1.27)	2.13 (0.71–6.36)	1.22 (0.54–2.76)	2.02 (0.75–5.47)	1.40 (0.43–4.61)
Decaffeinated coffee consumption						
None	1.00	1.00	1.00	1.00	1.00	1.00
≤1 cup/day	1.07 (0.79–1.45)	1.10 (0.77–1.57)	0.35 (0.10–1.20)	1.03 (0.48–2.24)	3.14 (1.28–7.69)	1.05 (0.40–2.80)
2 or more cups/day	0.71 (0.51–0.99)	0.67 (0.45–1.00)	0.54 (0.20–1.48)	1.38 (0.69–2.77)	1.45 (0.51–4.18)	0.50 (0.14–1.76)

OR, odds ratio; CI, confidence interval.

[a]*Each type of ovarian cancer is compared to all hospital-based noncancer controls (n = 828). Analysis based on 414 total ovarian cancer cases (255 serous, 33 mucinous, 49 endometrioid, 28 clear cell, and 27 borderline).*

[b]*Adjusted for age and residence.*

[c]*Adjusted for age, residence, and year of participation.*

However, caffeine administration in animals has also been associated with anticarcinogenic effects, particularly the inhibition of ultraviolet B-induced carcinomas in DMBA (7,12-dimethylbenz anthracene)-initiated SKH-1 mice[28]. Given the numerous mechanisms by which caffeine may influence cancer risk, it is difficult to draw firm conclusions about its likely role in ovarian cancer etiology. Nevertheless, our results suggest that the carcinogenic effects of caffeine may have overwhelmed the potentially protective effects of phytochemicals in more highly caffeinated beverages, such as regular coffee.

These findings are somewhat consistent with the epidemiologic evidence, which generally suggests a protective effect of decaffeinated coffee and black tea but not regular coffee. Although only three case–control studies have examined the association between decaffeinated coffee intake and ovarian cancer risk, one study identified a protective effect[20], another identified a statistically insignificant, but suggestive of a protective effect[14], and the third found no association[11]. Results have been similarly mixed for the association between black tea consumption and ovarian cancer risk. One cohort study identified a borderline protective effect for women consuming black tea[20], while another found no association[23]. Some case–control studies have identified a potential protective effect of black tea consumption on ovarian cancer risk[11,22], while others have not[14,15,21].

In contrast to tea and decaffeinated coffee, consumption of regular coffee has been previously associated with increased risk of ovarian cancer in several studies[8–14], although others have reported null findings[13, 15–20], and a recent study identified a protective effect[21]. A cohort study reported by Kuper *et al.*[13] suggested that this association may be modified by menopausal status; the study identified elevated ovarian cancer risk among premenopausal women only. That study also reported differences by histologic subtype, with increasing coffee intake resulting in linear risk elevations for mucinous tumors and borderline serous tumors only. Histologic subtypes were also examined in a population-based case–control study reported by Goodman *et al.*[14], which found that positive association between coffee consumption and cancer risk was more pronounced for mucinous than nonmucinous subtypes. Last, an Australian population-based case–control study reported a protective effect with increasing coffee consumption, and this effect was more pronounced for premenopausal women and for invasive tumors that were serous or endometrioid/clear cell[21]. Overall, many studies of ovarian cancer risk in relation to coffee or tea consumption have been limited by smaller samples than the current study[8–12,14,15,17–19,22], and it is possible that low power may explain some previous null findings. In addition, intake of some of the beverages under study was rare in some areas[16,20,22], limiting variability in exposure. As such, our study had several

advantages over many prior reports, including large sample size, information on intake of regular coffee, decaffeinated coffee, and black tea, and ability to examine associations by histologic subtype.

Despite these advantages, several methodologic issues should be considered in interpreting these results, including those inherent in case–control studies. All participants were treated at RPCI, a large regional cancer treatment center, and are not likely to represent the general population of either ovarian cancer patients or other patients in the region. However, it is unlikely that self-reported tea and coffee consumption would be systematically different at other facilities. The use of hospital controls can introduce bias if some controls suffered from conditions associated with coffee or tea consumption. However, results did not differ when associations were examined among subgroups of controls with common diagnoses (data not shown). In addition, only about 50% of eligible cases and controls agreed to complete the PEDS questionnaire; we have no way of ascertaining whether individuals who refused to participate differed from participants with respect to beverage consumption. Nevertheless, previous studies that used the PEDS database and faced the same methodologic issues consistently replicated established epidemiologic associations for a variety of cancer sites, including ovarian[29]. A potential benefit of using hospital-based controls is that it may decrease recall bias. Additionally, recall for common foods, such as coffee and tea, have been demonstrated to be good, further minimizing the risk of recall bias[30].

In summary, our results support a potential protective effect of tea consumption and decaffeinated coffee consumption on ovarian cancer risk; no effect was found for regular coffee consumption, potentially due to the higher caffeine content of this beverage. Large prospective studies in populations with variable consumption of caffeinated and decaffeinated beverages could help to disentangle the potential positive effects of phytochemicals in these beverages from the mixed effects of caffeine.

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