Coffee Consumption and Invasive Breast Cancer Incidence among Postmenopausal Women in the Cancer Prevention Study-II Nutrition Cohort

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ABSTRACT

Background: There is limited evidence of a potential inverse association between coffee, particularly caffeinated coffee, consumption and postmenopausal breast cancer risk, and few studies have examined this association by tumor hormone receptor status. To provide further evidence, we examined total, caffeinated, and decaffeinated coffee consumption in relation to postmenopausal invasive breast cancer incidence overall, and by tumor estrogen receptor (ER) and/or progesterone receptor (PR) subtype.

Methods: Among 57,075 postmenopausal women in the Cancer Prevention Study-II Nutrition Cohort who were cancer free and reported coffee intake in 1999, we identified 2,980 women diagnosed with invasive breast cancer during follow-up through June 2015. Multivariable-adjusted Cox proportional hazards regression was used to compute hazard ratios (HR) and 95% confidence intervals (CI).

Results: Neither total, caffeinated, nor decaffeinated coffee consumption was associated with invasive breast cancer risk; HRs (95% CIs) comparing consumption of ≥2 cups per day with <1 cup per month were 0.99 (0.89–1.11), 0.96 (0.87–1.06), and 1.06 (0.95–1.19), respectively. Similarly, coffee consumption was not associated with risk of hormone receptor–positive (ER^+ or PR^+) or hormone receptor–negative (ER^- and PR^-) breast tumors.

Conclusions: These findings do not support an association between coffee consumption and invasive breast cancer risk among postmenopausal women.

Impact: This large prospective study contributes to the limited evidence on coffee consumption and breast cancer risk, finding no association overall or by tumor receptor subtype.

Introduction

A 2017 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Continuous Update Project (CUP) systematic literature review showed a weak inverse association between coffee consumption and postmenopausal [hazard ratio (HR), 0.98; 95% confidence interval (CI), 0.95–1.00 per 1 cup/day], but not premenopausal (HR, 1.00; 95% CI, 0.97–1.03 per 1 cup/day) breast cancer risk (1). In the largest prospective study included in that analysis, the highest versus lowest category of caffeinated, but not decaffeinated, coffee consumption was associated with lower postmenopausal breast cancer risk (HR, 0.90; 95% CI, 0.82–0.98; ref. 2). Subsequently, at least two other studies found that coffee consumption was associated with lower risk of breast cancer–related mortality (3, 4). Despite accumulating evidence, the 2018 WCRF/AICR CUP comprehensive review classified the association as limited-no conclusion (5). To provide further evidence, we examined total, caffeinated, and decaffeinated coffee consumption in relation to postmenopausal invasive breast cancer incidence overall, and by tumor estrogen receptor (ER) and progesterone receptor (PR) status using data from the Cancer Prevention Study-II Nutrition Cohort (CPS-II NC).

Materials and Methods

Study population

The CPS-II NC is a prospective study of cancer incidence initiated in 1992 (6). Beginning in 1997, follow-up questionnaires were sent to participants every 2 years to ascertain updated and new exposure information, and self-reported new cancer diagnoses. The CPS-II NC has been approved by the Emory University Institutional Review Board (Atlanta, GA).

After excluding women who did not complete the 1999 survey (n = 14,297), were lost to follow-up (n = 3,125), reported a personal history of cancer other than nonmelanoma skin cancer prior to 1999 (n = 15,182), were not postmenopausal or aged 55+ years in 1999 (n = 286), and were missing both caffeinated and decaffeinated coffee consumption information (n = 7,817), 57,075 women were included in this analysis.

Assessment of coffee consumption

Coffee consumption was self-reported on the 1999 survey using a 152-item modified Harvard food frequency questionnaire (7). Usual intake of one cup of caffeinated and decaffeinated coffee (assessed separately) over the previous year was reported in one of 10 possible frequencies ranging from never to ≥6 per day. Participants who left either type of coffee blank (but not both), or whose reported consumption was never or <once per month were assigned 0 cups per day. Average cups of total coffee were calculated by summing the contribution from each type; categories

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Table 1. Means (SD) and distributions of sociodemographic, lifestyle, and other characteristics by total coffee consumption among women in 1999, CPS-II NC ($N = 57{,}075$).

	Total coffee consumption (cups/day)			
	Nondrinker ($n = 9{,}831$)	**<1 ($n = 11{,}787$)**	**1–<2 ($n = 12{,}849$)**	**≥2 ($n = 22{,}608$)**
Mean (SD)				
Total coffee (cups/day)	0.0 (0.0)	0.4 (0.3)	1.1 (0.2)	3.0 (1.0)
Caffeinated coffee (cups/day)	0.0 (0.0)	0.2 (0.3)	0.6 (0.5)	1.9 (1.4)
Decaffeinated coffee (cups/day)	0.0 (0.0)	0.2 (0.3)	0.5 (0.5)	1.1 (1.4)
Age in 1999 (years)	68.2 (6.4)	68.9 (6.3)	69.3 (6.2)	68.1 (6.0)
Body mass index in 1999 (kg/m^2)	26.1 (5.4)	26.0 (5.0)	25.8 (4.8)	25.7 (4.9)
Physical activity (MET hours/week)	14.4 (14.6)	14.8 (14.6)	14.6 (14.3)	15.1 (14.5)
American Cancer Society diet score	4.5 (2.0)	4.6 (1.9)	4.5 (1.9)	4.4 (1.9)
Age at menstruation (years)	12.7 (1.5)	12.7 (1.5)	12.7 (1.5)	12.7 (1.4)
Age at 1st live birth (years)	23.7 (3.9)	24.1 (4.0)	24.1 (4.0)	23.7 (3.8)
Distributions (%)				
White race	97.3	96.7	97.1	98.6
Ever cigarette smoker	29.7	39.7	44.0	52.4
Current alcohol drinker	26.7	45.3	51.6	59.9
Currently married	77.8	73.8	75.8	77.8
≤High school education	36.3	36.0	36.2	35.7
Positive family history of breast cancer	16.8	17.9	17.4	17.0
Positive personal history of breast cysts	39.5	39.4	38.5	38.8
Ever oral contraceptive use	39.6	37.7	38.2	41.4
Ever use of menopausal hormones	59.6	59.4	60.1	59.3
Routine mammography screening in 1999	84.7	87.1	87.7	86.4
Age at menopause less than 50 years	48.3	47.4	47.6	47.1
Nulliparous	6.9	7.6	8.0	6.9

Abbreviation: MET, metabolic equivalent.

were nondrinker (<1 cup/month), <1 cup/day, 1–<2 cups/day, and ≥2 cups/day.

Breast cancer ascertainment

We identified and verified (through medical record abstraction or linkage with state cancer registries or the National Death Index) 2,980 women with incident invasive breast cancer (International Classification of Disease for Oncology Third Editions site code C50) diagnosed between the date the 1999 questionnaire was returned and June 30, 2015. Hormone receptor status was available from medical records or state cancer registries.

Statistical analyses

Person-years of follow-up was calculated from the completion date of the 1999 questionnaire to breast cancer diagnosis (including censoring on *in situ* disease), death, last completed questionnaire, or June 30, 2015. Cox proportional hazards regression was used to calculate HRs and 95% CIs for total, caffeinated, and decaffeinated coffee consumption modeled as categorical and continuous variables. All models were stratified on single year of age and adjusted for confounding (see **Table 2** footnote). The proportional hazards assumption was assessed using likelihood ratio tests comparing multivariable-adjusted models with and without cross-product terms for follow-up time and coffee consumption; no violations were observed.

Associations of coffee consumption with risk of ER^+ or PR^+, or with ER^- and PR^- breast tumors were assessed using joint Cox proportional hazards regression analysis. All analyses were conducted using SAS (version 9.4).

Results

Among women in this analysis, 17.2% were noncoffee drinkers and 39.6% reported consuming ≥2 cups per day. Those in the highest category of total coffee consumption more frequently reported ever cigarette smoking and current alcohol drinking, whereas other potential confounding factors were similar across categories of coffee drinking (**Table 1**).

Neither total nor caffeinated coffee consumption was associated with postmenopausal invasive breast cancer risk in age- or in multivariable-adjusted models (**Table 2**). In age-adjusted analysis, consumption of ≥2 cups per day versus nondrinking of decaffeinated coffee was associated with a marginally statistically significant higher risk (HR, 1.12; 95% CI, 1.00–1.25). However, this association was attenuated in multivariable analysis (HR, 1.06; 95% CI, 0.95–1.19). There were no associations of coffee consumption with risk of ER/PR subtypes.

Discussion

Some epidemiologic (1) and mechanistic evidence (8) supports a potential inverse association between coffee consumption and breast cancer risk. However, in this large prospective study of postmenopausal women, among whom nearly 3,000 were diagnosed with invasive breast cancer over approximately 16 years of follow-up, we found no evidence that total, caffeinated, or decaffeinated coffee consumption was associated with a lower risk of invasive breast cancer overall or by ER/PR subtypes after adjusting for age, alcohol consumption, smoking history, and other breast cancer risk factors. These results may be useful in future meta-analyses of coffee and breast cancer risk.

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Table 2. HRs and 95% CIs for associations of total, caffeinated, and decaffeinated coffee consumption with risk of breast cancer overall and by hormone receptor subtype, CPS-II NC 1999–2015 ($N = 57{,}075$).

	Coffee consumption (cups/day)						
	Nondrinker ($n = 9{,}831$)	**<1 ($n = 11{,}787$)**	**1–<2 ($n = 12{,}849$)**	**≥2 ($n = 22{,}608$)**	**P_{trend}[a]**	**Per 1 cup/day**	***P***
All breast cancers ($N = 2{,}980$)							
Total coffee							
n, cases	494	573	685	1,228			
Age-adjusted HRs (95% CIs)	1.00 (ref)	0.97 (0.86–1.10)	1.06 (0.95–1.19)	1.06 (0.95–1.17)	0.15	1.02 (0.99–1.04)	0.23
Multivariable-adjusted HRs (95% CIs)[b]	1.00 (ref)	0.94 (0.83–1.06)	1.01 (0.90–1.14)	0.99 (0.89–1.11)	0.68	1.01 (0.98–1.03)	0.61
Caffeinated coffee							
n, cases	1,284	436	493	767			
Age-adjusted HRs (95% CIs)[c]	1.00 (ref)	0.94 (0.84–1.05)	1.10 (0.99–1.22)	1.00 (0.91–1.09)	0.83	1.00 (0.97–1.03)	0.93
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	0.92 (0.83–1.03)	1.08 (0.97–1.20)	0.96 (0.87–1.06)	0.61	0.99 (0.96–1.02)	0.58
Decaffeinated coffee							
n, cases	1,419	780	338	443			
Age-adjusted HRs (95% CIs)[c]	1.00 (ref)	0.97 (0.89–1.06)	0.94 (0.84–1.06)	1.12 (1.00–1.25)	0.05	1.04 (1.01–1.08)	0.02
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	0.96 (0.88–1.05)	0.91 (0.80–1.03)	1.06 (0.95–1.19)	0.30	1.03 (0.99–1.07)	0.15
ER or PR positive ($n = 2{,}392$)							
Total coffee							
n, cases	401	469	537	985			
Multivariable-adjusted HRs (95% CIs)[b]	1.00 (ref)	0.94 (0.82–1.08)	0.97 (0.85–1.10)	0.96 (0.85–1.09)	0.88	1.01 (0.98–1.04)	0.75
Caffeinated coffee							
n, cases	1,050	349	381	612			
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	0.90 (0.79–1.01)	1.01 (0.89–1.14)	0.93 (0.83–1.03)	0.28	0.98 (0.95–1.02)	0.38
Decaffeinated coffee							
n, cases	1,124	632	272	364			
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	0.97 (0.88–1.07)	0.91 (0.80–1.05)	1.08 (0.95–1.22)	0.29	1.03 (0.99–1.08)	0.16
ER and PR negative ($n = 302$)							
Total coffee							
n, cases	46	59	78	119			
Multivariable-adjusted HRs (95% CIs)[b]	1.00 (ref)	1.07 (0.72–1.57)	1.30 (0.90–1.88)	1.11 (0.78–1.57)	0.80	1.00 (0.92–1.08)	0.89
Caffeinated coffee							
n, cases	122	52	59	69			
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	1.16 (0.84–1.62)	1.41 (1.03–1.93)	0.97 (0.71–1.32)	0.80	0.99 (0.90–1.09)	0.95
Decaffeinated coffee							
n, cases	137	84	38	43			
Multivariable-adjusted HRs (95% CIs)[b,c]	1.00 (ref)	1.06 (0.81–1.40)	1.05 (0.73–1.52)	1.10 (0.78–1.56)	0.64	1.03 (0.92–1.15)	0.99

Abbreviation: MET, metabolic equivalent.

[a]P_{trend} was calculated using a continuous variable created from the medians within each category of consumption.

[b]Multivariable models included body mass index (15–<18.5, 18.5–<25, 25–<30, 30+ kg/m^2, and missing), race (white, black, and other/missing), physical activity (<8.75, 8.75–17.5, >17.5 MET-hours/week, and unknown), parity (no live births, 1–2, 3+ live births, and unknown), personal history of benign breast disease (no and yes), family history of breast cancer (no and yes), cigarette smoking history [never smoker, former (<10, 10–<20, 20–<30, 30+, and missing years since quit), and current (<20, 20–<40, 40+, and missing cigarettes per day)], age at menopause (<45, 45–<50, 50–53, 54+ years, and unknown), menopausal hormone use (never, former, current, and unknown), mammography screening in 1999 (none, routine screening, symptomatic screening, both routine and symptomatic, and unknown), and alcohol consumption (nondrinker, <1 drink/week, 1–<7 drinks/week, 1–<2 drinks/day, 2+ drinks/day, and unknown).

[c]Caffeinated and decaffeinated coffee consumption were mutually adjusted.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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S.M. Gapstur: Conceptualization, supervision, methodology, writing–original draft. **M.M. Gaudet:** Methodology, writing–review and editing. **Y. Wang:** Methodology, writing–review and editing. **R.A. Hodge:** Formal analysis, methodology, writing–review and editing. **C.Y. Um:** Writing–review and editing. **T.J. Hartman:** Writing–review and editing. **M.L. McCullough:** Data curation, methodology, writing–review and editing.

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