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# Coffee and black tea consumption and breast cancer mortality in a cohort of Swedish women

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BACKGROUND: Coffee and black tea contain a mixture of compounds that have the potential to influence breast cancer risk and survival. However, epidemiologic data on the relation between coffee and black tea consumption and breast cancer survival are sparse.

METHODS: We investigated the association between coffee and black tea consumption and survival among 3243 women with invasive breast cancer in the Swedish Mammography Cohort. Intake was estimated using a food frequency questionnaire. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs).

RESULTS: From 1987 to 2010 there were 394 breast cancer-specific deaths and 973 total deaths. Coffee and black tea were not associated with breast cancer-specific or overall mortality. Women consuming 4+ cups of coffee per day had a covariate and clinical characteristics-adjusted HR (95% CI) of death from breast cancer of 1.14 (0.71–1.83; $p_{trend} = 0.81$) compared with those consuming <1 cup per day. Women consuming 2+ cups of black tea per day had a covariate and clinical characteristics-adjusted HR (95% CI) of death from breast cancer of 1.02 (0.67–1.55; $p_{trend} = 0.94$) compared with non-tea drinkers. Caffeine was also not associated with breast cancer-specific (HR for top to bottom quartile = 1.06; 95% CI = 0.79–1.44; $p_{trend} = 0.71$) or overall mortality.

CONCLUSION: Our findings suggest that coffee, black tea, and caffeine consumption before breast cancer diagnosis do not influence breast cancer-specific and overall survival.

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Coffee and black tea contain a mixture of compounds that have the potential to influence breast cancer risk and survival. Coffee may influence risk and progression through the inhibition of DNA methylation (Lee and Zhu, 2006), influences on tumour differentiation (Pozner *et al*, 1986), or alterations in sex hormone levels (Ferrini and Barrett-Connor, 1996; Nagata *et al*, 1998). Black tea has also been shown to alter sex hormone levels (Kuruto-Niwa *et al*, 2000; Wu *et al*, 2005), and the flavonoids it contains may have antioxidant effects (Trevisanato and Kim, 2000). Caffeine is found in both coffee and black tea, and in rodents has been shown to increase mammary cell differentiation (VanderPloeg *et al*, 1992) and decrease tumour incidence (Petrek *et al*, 1985). Conversely, caffeine has also been associated with increased mammary tumours in animal models (Welsch *et al*, 1983).

Coffee consumption and breast cancer risk have been extensively studied with conflicting results (Ishitani *et al*, 2008; Bissonauth *et al*, 2009; Larsson *et al*, 2009a; Tang *et al*, 2009; Bhoo Pathy *et al*, 2010; Boggs *et al*, 2010; Nilsson *et al*, 2010; Fagherazzi *et al*, 2011; Gierach *et al*, 2011; Li *et al*, 2011). However, to our knowledge, only one observational study has examined coffee consumption and survival following breast cancer diagnosis (Sugiyama *et al*, 2010), and no studies have examined black tea or caffeine. In this study, we investigated whether pre-diagnosis coffee, black tea, and caffeine intake were associated with breast cancer survival among women diagnosed with invasive breast cancer in the population-based Swedish Mammography Cohort (SMC). We also examined whether the association between coffee, black tea, or caffeine and survival differed by hormone receptor status, disease stage at diagnosis, or smoking status.

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## MATERIALS AND METHODS

### Study population

This study included 3243 participants in the SMC with invasive breast cancer diagnosed from 1987 to 2010. Recruitment and characteristics of this cohort have been previously described (Wolk *et al*, 2006). In brief, the SMC is a population-based cohort of 66 651 women born between 1914 and 1948 that were recruited between 1987 and 1990 in Västmanland and Uppsala counties in central Sweden. Participants completed a baseline questionnaire with questions regarding diet, reproductive, and other factors. In 1997, a second questionnaire was extended to include dietary supplements, physical activity, and smoking status, and was sent to participants who were still alive and residing in the study area; 39 227 (70%) women returned this questionnaire. The study was approved by the ethics committee at the Karolinska Institutet.

Histologically confirmed incident invasive breast cancer cases were ascertained by linkage of the study cohort with the Swedish Cancer Registry. This registry has been estimated to

provide almost 100% complete case ascertainment (Mattsson and Wallgren, 1984). Oestrogen receptor (ER) and progesterone receptor (PR) status and other clinical characteristics were obtained by reviewing pathology laboratory works logs from Uppsala University Hospital and by linkage with the clinical database at the Regional Oncology Centre in Uppsala. Oestrogen and PR status, menopausal status at diagnosis, tumour size, grade, lymph node involvement, and type of treatment were available for ~72% of the cases. More detailed information on the evaluation of hormone receptor status in this cohort has been described previously (Larsson *et al*, 2009b).

### Dietary assessment

Diet was assessed using a 67-item food frequency questionnaire (FFQ) at baseline and a 96-item FFQ in 1997. Participants were asked how often, on average, they had consumed coffee and tea during the previous 6 months (1987) or year (1997). Eight responses were possible ranging from never or seldom to four or more times per day. Decaffeinated coffee and tea were rarely consumed in Sweden during the study period. As the majority of tea consumed during the study period was black tea, we refer to tea as black tea throughout the manuscript. Caffeine intake was calculated by summing the caffeine content of coffee and tea multiplied by the amount of consumption using values obtained from the Swedish National Food Administration Database. The FFQ has been previously validated among SMC participants with correlation coefficients between the questionnaire and four 1-week dietary records of 0.6 for coffee and 0.8 for tea (A Wolk, unpublished data, 1992).

### Outcome assessment

Date of death was identified through linkage to the Swedish National Death Registry at Statistics Sweden. Cause of death was determined by International Classification of Diseases (ICD) codes (ICD9 and ICD10) through linkage to the Cause of Death Registry at the National Bureau of Health and Welfare.

### Statistical analysis

Cox proportional hazard models with time since diagnosis in months as the time scale were used to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for death from breast cancer. Participants contributed person-time from the date of breast cancer diagnosis until death from breast cancer (primary endpoint), death from another cause, or end of follow-up on 16 October 2010. Secondary analyses were conducted with death from any cause as the endpoint. Coffee consumption was categorised as $<1$ (reference), 1, 2–3 and $\geqslant 4$ cups per day. Black tea consumption was categorised as non-drinker (reference), $<1$, 1 cup per day, and $\geqslant 2$ cups per day. Caffeine intake was categorised in quartiles with the lowest quartile as the reference group. Total caloric intake and age at diagnosis were included in all models.

Education level, marital status, menopausal status at diagnosis, body mass index (BMI), alcohol intake, and calendar year of diagnosis were included in all multivariable models. Additional multivariable models were adjusted for the following clinical characteristics: stage, grade, radiation treatment, and chemotherapy/hormonal therapy. Additional adjustment for the clinical covariates tumour size and number of positive lymph nodes did not further alter the effect estimates; thus they were not included in the final model. We also adjusted for physical activity (Holmes *et al*, 2005) and smoking status among women who completed the 1997 questionnaire. Coffee and black tea were included simultaneously in all models. Tests for linear trend were performed by assigning the median value of each category to each participant in that group.

We examined whether the association between coffee, black tea, and caffeine consumption and breast cancer survival differed by hormone receptor status, disease stage at diagnosis, or smoking status with a likelihood ratio test comparing the model with the cross-product term between each exposure variable and each potential effect modifier to the model with main effects only. All tests of statistical significance were two-sided, and statistical analyses were performed using SAS Version 9.2 (SAS Institute Inc., Cary, NC, USA).

## RESULTS

During 28 676 person-years of follow-up contributed by 3243 breast cancer cases, there were 973 deaths with 394 deaths from breast cancer. Ninety-six percentage of participants reported any coffee consumption and seventy-three percentage reported any black tea consumption. Among those consuming coffee or black tea, the median consumption among the drinkers was 2.5 and 1.0 cups per day, respectively. Median caffeine consumption among all participants was 326 mg per day. Women consuming $\geqslant 4$ cups of coffee per day tended to be younger, had a lower mean BMI, were less often nulliparous, consumed more alcohol, consumed less black tea, and were more likely to smoke than those in lower categories of coffee intake (Table 1).

No association was observed between coffee consumption and breast cancer-specific or overall mortality. Women consuming $\geqslant 4$ cups of coffee per day had a covariate-adjusted HR (95% CI) of death from breast cancer of 1.01 (0.64–1.61) compared with those consuming $<1$ cup per day ($p_{\text{trend}} = 0.99$). Adjustment for clinical characteristics (breast cancer stage and grade) and treatment did not materially alter the results (1.14 (0.71–1.83); $p_{\text{trend}} = 0.81$). Results were similar when death from any cause was the outcome (Table 2). When coffee consumption was dichotomised, comparing women consuming $\geqslant 1$ cup per day to those consuming $<1$ cup per day there was no association with breast cancer-specific (HR = 1.17; 95% CI 0.80–1.72) or overall mortality (HR = 1.02; 95% CI 0.81–1.29). Caffeine intake was not associated with breast cancer-specific (HR for top (median intake 488 mg per day) to bottom (median intake 155 mg per day) quartile = 0.99; 95% CI = 0.74–1.33; $p_{\text{trend}} = 0.93$) or overall mortality (HR for top to bottom quartile = 1.07; 95% CI = 0.88–1.30; $p_{\text{trend}} = 0.67$).

Black tea consumption was nonsignificantly inversely associated with breast cancer-specific and overall mortality. Compared with women consuming no black tea those consuming $\geqslant 2$ cups per day had a covariate-adjusted HR (95% CI) of death from breast cancer of 0.87 (0.58–1.32; $p_{\text{trend}} = 0.58$) and 0.84 for total deaths (0.64–1.09; $p_{\text{trend}} = 0.39$). Adjustment for clinical characteristics and treatment attenuated the results (HR for breast-cancer deaths = 1.02; 95% CI = 0.67–1.55; $p_{\text{trend}} = 0.94$ and total deaths = 0.94; 95% CI = 0.72–1.23; $p_{\text{trend}} = 0.88$) (Table 3). When women with any black tea consumption were compared with those with no black tea consumption, no association was observed with breast cancer-specific (HR = 0.98; 95% CI 0.78–1.22) or overall mortality (HR = 0.94; 95% CI 0.82–1.09).

The associations between coffee, black tea, and caffeine intake and mortality did not vary by hormone receptor status (Supplementary Tables 1 and 2), disease stage at diagnosis, or smoking (results not shown) (all $P > 0.05$). In addition, adjustment for ER/PR status in the covariate and clinical characteristics model did not materially change the results. In a sensitivity analysis that excluded women with stage IV breast cancer, results were not materially different. We also adjusted for physical activity and smoking status in the subset of women who completed the 1997 questionnaire and saw no material change in the effect estimates.

We examined dietary change following breast cancer diagnosis among the 691 breast cancer cases who were diagnosed with breast cancer from 1987 to 1996 and completed a FFQ in 1997 after their

**Table 1** Characteristics of 3234 women with invasive breast cancer in the Swedish Mammography Cohort by coffee intake[a]

| | Coffee intake (cups per day) | | | |
|---|---|---|---|---|
| | <1 | 1 | 2–3 | ⩾4 |
| Median coffee intake (g per day) | 12 | 177 | 443 | 768 |
| Age at enrollment (years) | 52.4 | 56.1 | 53.1 | 48.5 |
| Age at diagnosis (years) | 65.6 | 68.6 | 65.8 | 62.1 |
| Post-secondary education (%) | 16.8 | 14.3 | 13.0 | 14.4 |
| Married (%) | 65.3 | 68.6 | 71.7 | 71.3 |
| Body mass index (kg m$^{-2}$) | 25.2 | 25.2 | 24.9 | 24.7 |
| Height (cm) | 165.3 | 164.9 | 164.5 | 165.1 |
| Age at menarche (years) | 13.2 | 13.3 | 13.2 | 13.1 |
| Nulliparous (%) | 14.2 | 17.5 | 11.7 | 11.2 |
| Age at first birth among parous women (years) | 24.6 | 24.9 | 24.8 | 23.7 |
| Number of children | 2.3 | 2.3 | 2.2 | 2.4 |
| Family history of breast cancer (%) | 10.6 | 13.9 | 10.7 | 9.5 |
| Ever use of oral contraceptives (%) | 58.7 | 48.6 | 55.8 | 63.7 |
| Ever use of postmenopausal hormones (%) | 46.8 | 51.3 | 45.8 | 47.1 |
| Postmenopausal at diagnosis (%) | 91.2 | 94.6 | 91.2 | 89.2 |
| Alcohol intake (grams per day) | 2.2 | 2.4 | 2.9 | 3.4 |
| Current smoker (%)[b] | 5.9 | 5.8 | 11.8 | 24.8 |
| Past smoker (%)[b] | 32.5 | 31.0 | 33.6 | 43.3 |
| Tea intake (cups per day) | 1.3 | 0.9 | 0.5 | 0.3 |
| Caffeine intake (mg per day) | 105.5 | 175.1 | 338.7 | 523.1 |
| Total energy intake (kcal per day) | 1532 | 1498 | 1587 | 1688 |
| *Disease stage (%)*[c,d] | | | | |
| Stage I | 51.7 | 50.2 | 52.5 | 54.1 |
| Stage II | 42.9 | 42.2 | 40.0 | 39.7 |
| Stage III/IV | 3.9 | 6.9 | 5.5 | 5.2 |
| *Treatment (%)*[d,e] | | | | |
| Radiation | 56.6 | 48.2 | 52.3 | 56.6 |
| Chemotherapy | 21.2 | 12.3 | 13.1 | 17.2 |
| Hormonal | 33.6 | 33.9 | 32.1 | 32.1 |
| Oestrogen receptor positive (%)[d] | 79.7 | 83.0 | 81.4 | 81.7 |
| Progesterone receptor positive (%)[d] | 67.2 | 70.4 | 66.5 | 65.4 |
| *Tumour size (%)*[d] | | | | |
| <2 cm | 66.0 | 59.5 | 60.9 | 63.7 |
| 2–4 cm | 28.1 | 33.2 | 33.3 | 29.6 |
| >4 cm | 5.9 | 7.2 | 5.7 | 6.6 |
| *Number of positive-lymph nodes (%)*[d] | | | | |
| None | 57.6 | 63.8 | 65.6 | 65.3 |
| 1–3 | 27.3 | 25.8 | 22.9 | 23.2 |
| ⩾4 | 15.1 | 10.5 | 11.6 | 11.5 |

[a]Data represent mean unless otherwise indicated. [b]Smoking status was only available from women ($n=2110$) who completed the 1997 questionnaire. [c]Percentages may not equal 100 owing to missing values. [d]Information on clinical characteristics was available for ~72% of the participants. [e]Greater than 100% because some breast cancer patients received more than one treatment.

breast cancer diagnosis. Over 90% remained in the same or adjacent category of coffee or black tea intake following their breast cancer diagnosis. However, numbers were too small to examine the association between post-diagnosis coffee or black tea intake and survival in this group.

## DISCUSSION

In this prospective study of Swedish women with breast cancer, we observed no association between coffee, primarily black tea, or caffeine intake and mortality following breast cancer diagnosis. This lack of association was consistent across hormone receptor subtypes, stage of diagnosis, and among both smokers and non-smokers.

The epidemiologic data regarding the relation between coffee, tea, and caffeine and breast cancer survival is limited. Stocks compared age-adjusted death rates and annual consumption of tea and coffee in 20 countries and reported a positive association between tea and breast cancer death rates but no association with coffee (Stocks, 1970). To our knowledge, no observational studies have examined the association between tea or caffeine consumption and breast cancer survival, and only one study has examined the association with coffee consumption. Sugiyama *et al* (2010) examined coffee consumption and mortality due to all-cause, cardiovascular disease (CVD), and cancer in a prospective cohort study in Japan. They observed an inverse association between coffee consumption and overall and CVD mortality, but no association with total cancer mortality or breast cancer-specific mortality (HR (95% CI) for breast cancer-specific mortality for 1 cup per day *vs* none $=1.54$ (0.34–6.93)); however, the breast cancer-specific results were based on only 19 deaths. Coffee intake was much lower among this population than in Sweden, which has one of the highest consumption rates in the world. Despite the different ranges of coffee consumption between the two study populations, we also did not observe a significant association between coffee intake and breast cancer mortality.

In the SMC, we have previously reported no association between coffee consumption and breast cancer risk and an increased risk of overall breast cancer as well as an increased risk for ER+/PR+ tumours with black tea consumption (Larsson *et al*, 2009a). The positive association between black tea consumption and hormone receptor-positive breast cancer risk may indicate a role of sex steroid hormones as *in vitro* studies have demonstrated that tea catechins exhibit oestrogenic activity in low concentrations (Kuruto-Niwa *et al*, 2000). The lack of association observed between black tea consumption and mortality suggests that consumption of black tea may influence breast cancer incidence and survival through different mechanisms.

A limitation of our study was for the majority of our participants we only had a pre-diagnosis assessment of diet and thus had limited power to examine diet post diagnosis during the follow-up period. Among a cohort of breast cancer patients in the United Kingdom, small but statistically significant changes in pre- to post-diagnosis intake of coffee (pre-diagnosis mean 1.05 servings per day and post-diagnosis mean 0.96 servings per day) and tea (pre-diagnosis mean 1.55 servings per day and post-diagnosis mean 1.61 servings per day) were observed (Velentzis *et al*, 2011). However, 90% of our participants who completed an FFQ post diagnosis remained in the same or adjacent category of coffee and black tea consumption following diagnosis. In addition, other dietary or lifestyle factors may have changed following breast cancer diagnosis. Studies have shown that younger women are most likely to report these changes and the average age at breast cancer diagnosis in our cohort was 65.1 years (Salminen and Lagstrom, 2000; Maunsell *et al*, 2002). Coffee and black tea consumption were assessed with a self-administered FFQ, which is subject to some measurement error and could have resulted in attenuation of the true association. However, in this cohort the FFQ has been validated using diet records with correlations of 0.6 for coffee and 0.8 for tea (A Wolk, unpublished data, 1992). Finally, residual or unmeasured confounding by lifestyle or other dietary factors that are associated with coffee and/or tea consumption is a possibility. However, we adjusted for a number of potential confounders including smoking status, and the association did not materially change.

To our knowledge, this is the largest study among women with breast cancer to examine the association between coffee consumption and mortality, and the first study to examine the association with primarily black tea and caffeine. With 973 total deaths, including 394 breast cancer deaths, we had the ability to examine breast cancer-specific mortality as well as how the associations

**Table 2** Hazard ratios (HR) and 95% confidence intervals (95% CIs) of breast cancer death by coffee intake among 3234 invasive breast cancer cases in the Swedish Mammography Cohort

| | Coffee intake (cups per day) | | | | |
|---|---|---|---|---|---|
| | **<1** | **1** | **2–3** | **⩾4** | **$P_{trend}$[a]** |
| Coffee | | | | | |
| Person-years | 2359 | 3793 | 17 309 | 5216 | |
| *Breast cancer deaths* | 30 | 58 | 246 | 60 | |
| Age-adjusted model | 1.00 | 1.16 (0.74–1.82) | 1.10 (0.75–1.63) | 0.92 (0.58–1.45) | 0.48 |
| Covariate-adjusted model[b] | 1.00 | 1.08 (0.69–1.69) | 1.10 (0.74–1.62) | 1.01 (0.64–1.61) | 0.99 |
| Covariate-adjusted model + clinical characteristics[c] | 1.00 | 1.23 (0.78–1.93) | 1.19 (0.79–1.79) | 1.14 (0.71–1.83) | 0.81 |
| *Total deaths* | 79 | 161 | 596 | 137 | |
| Age-adjusted model | 1.00 | 0.99 (0.76–1.30) | 0.97 (0.76–1.23) | 1.02 (0.76–1.36) | 0.99 |
| Covariate-adjusted model[b] | 1.00 | 0.98 (0.74–1.28) | 0.97 (0.76–1.24) | 1.08 (0.81–1.44) | 0.61 |
| Covariate-adjusted model + clinical characteristics[c] | 1.00 | 1.00 (0.76–1.32) | 1.00 (0.78–1.28) | 1.12 (0.84–1.51) | 0.45 |

[a]Determined using category medians. [b]Cox proportional hazard model adjusted for age (continuous), energy intake (continuous), education level (primary, high school, and university), marital status (single, married, divorced, widowed, and living with partner), menopausal status at diagnosis (premenopausal, postmenopausal, and unknown), body mass index (<20, 20–24.9, 25–29.9, and ⩾30 kg m$^{-2}$), alcohol intake (non-drinker, <3.4, 3.4–9.9, ⩾10 g per day), and calendar year of diagnosis (continuous). [c]Cox proportional hazard model adjusted for the variables above plus disease stage (I, II, and III/IV), grade (I, II, and III), radiation treatment (yes/no), and chemotherapy and/or hormonal treatment (no chemotherapy or hormonal treatment, hormonal therapy and no chemotherapy, chemotherapy and no hormonal therapy, and hormonal therapy and chemotherapy).

**Table 3** Hazard ratios (HR) and 95% confidence intervals (95% CIs) of breast cancer death by tea intake among 3234 invasive breast cancer cases in the Swedish Mammography Cohort

| | Tea intake (cups per day) | | | | |
|---|---|---|---|---|---|
| | **0** | **<1** | **1** | **⩾2** | **$P_{trend}$[a]** |
| Tea | | | | | |
| Person-years | 7716 | 10 267 | 7930 | 2764 | |
| *Breast cancer deaths* | 120 | 136 | 105 | 33 | |
| Age-adjusted model | 1.00 | 0.84 (0.65–1.07) | 0.84 (0.65–1.10) | 0.78 (0.52–1.16) | 0.29 |
| Covariate-adjusted model[b] | 1.00 | 0.93 (0.72–1.19) | 0.93 (0.71–1.22) | 0.88 (0.58–1.32) | 0.58 |
| Covariate-adjusted model + clinical characteristics[c] | 1.00 | 0.96 (0.75–1.23) | 0.98 (0.75–1.28) | 1.02 (0.67–1.55) | 0.94 |
| *Total deaths* | 303 | 335 | 260 | 75 | |
| Age-adjusted model | 1.00 | 0.84 (0.72–0.98) | 0.87 (0.73–1.03) | 0.79 (0.61–1.03) | 0.20 |
| Covariate-adjusted model[b] | 1.00 | 0.90 (0.77–1.06) | 0.94 (0.79–1.11) | 0.84 (0.64–1.09) | 0.39 |
| Covariate-adjusted model + clinical characteristics[c] | 1.00 | 0.94 (0.80–1.10) | 0.97 (0.82–1.15) | 0.94 (0.72–1.23) | 0.88 |

[a]Determined using category medians. [b]Cox proportional hazard model adjusted for age (continuous), energy intake (continuous), education level (primary, high school, and university), marital status (single, married, divorced, widowed, and living with partner), menopausal status at diagnosis (premenopausal, postmenopausal, and unknown), body mass index (<20, 20–24.9, 25–29.9, ⩾30 kg m$^{-2}$), alcohol intake (non-drinker, <3.4, 3.4–9.9, and ⩾10 g per d), and calendar year of diagnosis (continuous). [c]Cox proportional hazard model adjusted for the variables above plus disease stage (I, II, and III/IV), grade (I, II, and III), radiation treatment (yes/no), and chemotherapy and/or hormonal treatment (no chemotherapy or hormonal treatment, hormonal therapy and no chemotherapy, chemotherapy and no hormonal therapy, and hormonal therapy and chemotherapy).

differed by tumour hormone receptor status. We had 80% power to detect hazards ratios of 1.38. We also have complete follow-up of all cases, a long follow-up period, detailed information on diet, and data on many important covariates, including clinical and lifestyle characteristics.

In conclusion, among a population of Swedish women with high coffee consumption, we did not observe an association between coffee, black tea, or caffeine consumption and breast cancer-specific survival or overall survival.

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