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**File: ■ Coffee (*Coffea arabica*)**

**■ Breast Cancer**

**■ Hormone- and Non-hormone-responsive Tumors**

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**RE: Coffee Consumption Lowers Risk for Non-hormone-responsive Breast Cancer Subtypes**

Li J, Seibold P, Chang-Claude J, et al. Coffee consumption modifies risk of estrogen-receptor negative breast cancer. *Breast Cancer Res.* 2011;13(3):R49. doi: 10.1186/bcr2879.

Breast cancer can be divided into hormone-responsive (estrogen receptor [ER]-positive) and non-hormone-responsive (ER-negative) subtypes. Some reports suggest that heterogeneity exists in the associations between coffee (*Coffea arabica*) consumption and breast cancer risk, according to the two subtypes. The authors assessed the association between coffee consumption and postmenopausal breast cancer risk in a large population-based study overall and stratified by ER tumor subtypes.

Coffee, a complex mixture of caffeine and polyphenols, has been shown in experimental studies to alter cancer risk. Experimental and clinical studies have suggested that it can play a dual role as both a carcinogen, in which it inhibits cellular repair of DNA or enhances cell proliferation, and a chemopreventive agent with antioxidative and estrogenic properties. Most studies suggest that high coffee consumption is associated with a modest reduction of breast cancer risk.

Subjects were drawn from a population-based case-control study described previously.<sup>1</sup> The parent study included women aged 50 to 74 years born in Sweden and living there between October 1, 1993 and March 31, 1995. The authors attempted to contact all incident cases of invasive breast cancer in this study group. Included in their study were 2,818 women with breast cancer and 3,111 controls.

For the validation analysis, data were collected from the Mamma Carcinoma Risk Factor Investigation (MARIE),<sup>2</sup> carried out from August 2002 to September 2005 in two study regions in Germany. It included 3,464 postmenopausal women aged 50 to 74 years with primary invasive or in situ breast tumors and 6,657 controls.

The authors collected data by means of an extensive mailed questionnaire requesting detailed information on established and possible breast cancer risk factors, including

reproductive and menstrual history, family history of breast cancer, hormone replacement therapy (HRT), and anthropometric measures. Lifestyle information (such as smoking, alcohol intake, and physical activity) and data on coffee consumption one year before the interview (specified in cups per week [one cup equivalent to 1.5 dL]) were also collected.

ER and progesterone receptor (PR) content of breast tumors was routinely measured in Sweden at the time of the study but not for tumors  $\leq 1$  cm in size. Therefore, the quantitative receptor content (both ER and PR) was available for only 65.4% (1,835 women) of the tumors.

For the MARIE study, information on potential risk factors for breast cancer was obtained in a face-to-face interview using a standardized questionnaire. The consumption of caffeine-containing coffee was calculated in cups per day and frequency. The analysis included only those women who answered both questions on portion size and frequency of coffee consumption. The final study group included 5,395 controls and 2,651 cases. Information on the ER and PR status of tumors was obtained from medical records.

The authors estimated odds ratios and corresponding 95% confidence intervals (CIs) by using the multivariate logistic regression models fitted to examine breast cancer risk in a stratified case-control analysis. Heterogeneity among ER subtypes was evaluated in a case-only analysis, treating ER status as a dependent variable and including coffee consumption as a covariate.

The authors report that in both studies, the age at menarche was weakly but positively associated with breast cancer ( $P=0.057$  in the Swedish samples and  $P=0.0026$  in the MARIE samples). Family history of breast cancer, age at menopause, parity, age of first birth, recent body mass index, use of HRT, alcohol consumption, physical activity, and highest education level attained were strongly significant for breast cancer risk.

The variables found to be significantly associated with coffee consumption among controls in the Swedish study were HRT ( $P=0.008$ ), smoking ( $P<0.0001$ ), and highest education level attained ( $P=0.041$ ).

In the Swedish study, coffee consumption was associated with a modest decrease in overall breast cancer risk in the age-adjusted model. The authors' main finding was that the breast cancer risk reduction associated with higher coffee consumption was significantly higher for ER-negative compared with ER-positive tumors ( $P$  heterogeneity [age-adjusted]=0.004). This effect was independent of HRT, smoking, highest education level attained, and average daily alcohol consumption.

In the multivariate-adjusted Swedish study, women who drank more than five cups of coffee per day were 57% ( $P=0.0003$ ) and 33% ( $P=0.034$ ) less likely to get the ER-negative and PR-negative disease, respectively, than the reference group.

The authors attempted to validate the trend test results of the Swedish ER-negative breast cancer subgroup by examining the results of the MARIE study. Though not reaching statistical significance, the strongest protective effect from heavy coffee consumption was similarly observed for the ER-negative subtype.

The authors believe that, collectively, "the results from the two studies in this paper support a protective effect of high intakes of coffee against ER-negative breast cancer. The weaker associations found in the MARIE study may perhaps be attributed to other factors related to coffee drinking, such as brewing method, bean type, and caffeine content."

The authors cite several other studies that examined the relationship between direct measurements of coffee consumption or related variables and risk for ER-positive and ER-negative breast cancers. While not finding any evidence that coffee consumption increases the overall risk for postmenopausal breast cancer, a high daily intake of coffee was associated with a significant decrease in ER-negative breast cancer among postmenopausal women. "Future studies are needed to confirm the effects of coffee consumption in the light of breast cancer subtypes."

—*Shari Henson*

#### **References**

<sup>1</sup>Magnusson C, Baron J, Persson I, et al. Body size in different periods of life and breast cancer risk in postmenopausal women. *Int J Cancer*. 1998;76(1):29-34.

<sup>2</sup>Flesch-Janys D, Slinger T, Mutschelknauss E, et al. Risk of different histological types of postmenopausal breast cancer by type and regimen of menopausal hormone therapy. *Int J Cancer*. 2008;123(4):933-941.

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