Null Results in Brief

Cigarette Smoking Is Not Associated with Breast Cancer Risk in Young Women

Jennifer Prescott,[1] Huiyan Ma,[1] Leslie Bernstein,[1] and Giske Ursin[1,2]

[1]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California and [2]Department of Nutrition, University of Oslo, Oslo, Norway

Introduction

Cigarette smoking has been hypothesized to have a carcinogenic effect on breast tissue, particularly when exposure occurs before sexual maturity and breast tissue differentiation (1). Epidemiologic studies of cigarette smoking on breast cancer risk during this developmental period have produced inconsistent results (2-14). However, recent cohort studies (7-10), including two with mainly young women (7, 10), suggest an effect of smoking at an early age. In this study, we examine the effect of smoking on breast cancer risk in women <50 years of age.

Materials and Methods

Details of this population-based case-control study have been described elsewhere (15). Briefly, 1,794 U.S.-born, English-speaking, non-Hispanic white, Hispanic white, and African-American Los Angeles female residents with incident invasive breast cancer, ages 20-49 years, were recruited through the Los Angeles County Cancer Surveillance Program between February 1998 and May 2003. Four hundred forty-four U.S.-born, English-speaking neighborhood controls matched by age ($\pm$5 years) and race were recruited between July 2000 and March 2003. After excluding subjects due to missing information, 1,728 cases and 441 controls remained in our analysis.

In-person interviews were conducted using a structured questionnaire to gather information on reproductive history, smoking and alcohol consumption, family history of breast and ovarian cancer, demographics, and other factors. Information was recorded up to the reference date for each subject. The reference date was the date of diagnosis for cases or the date of initial household contact for controls. All study participants signed an informed consent before interview. The study protocol was approved by the University of Southern California's Institutional Review Board.

Data Analyses. We used unconditional multivariable logistic regression to estimate the odds ratios and 95% confidence intervals as a measure of breast cancer risk associated with cigarette use. We adjusted for age, race, education, age at menarche, number of full-term pregnancies, age at first full-term pregnancy, average amount of alcohol within the recent 5-year period, and family history of breast or ovarian cancer. Additional analyses restricted to cases diagnosed after June 2000 yielded similar results (data not shown). We also conducted a case-case analysis to determine whether family history modifies the association between smoking and breast cancer risk. Statistical analyses were done using the SAS version 9 statistical package (SAS Institute, Cary, NC).

Results

Compared with women who never smoked, women who reported having ever smoked were not at increased risk for breast cancer (odds ratio, 0.99; 95% confidence interval, 0.78-1.25; Table 1). Likewise, no statistically significant association or trend with breast cancer risk was found for total years of smoking; age commenced smoking; lifetime average cigarettes smoked; average number of cigarettes smoked in recent 5 years or in the 5-year period after menarche, before 18 years of age, or before age at first birth; or total years of smoking before first full-term pregnancy (all trend P values were >0.25). Results were similar when we restricted the analysis to long-term smokers (20+ years) and never smokers (data not shown). We observed no significant trends between smoking and risk of breast cancer when we restricted analyses to stage I, II, or III/IV cancer cases (data not shown).

First-degree family history of breast or ovarian cancer did not modify the association between any of the smoking variables and breast cancer risk ($P > 0.15$).

Discussion

In this study of young women (<50 years), we did not find significant associations of breast cancer risk with any of the smoking characteristics investigated. Our results are consistent with the bulk of published literature on this topic, which do not find significant relationships between smoking and overall incident invasive breast cancer risk among young or premenopausal women (3-5, 16-21). A review of the literature by IARC (22) and a pooled analysis on breast cancer and smoking by the Collaborative Group on Hormonal Factors in Breast Cancer (23) both conclude that there is no overall association between smoking and breast cancer risk. On the other hand, four recent studies have found an effect of smoking at an early age and breast cancer risk (7-10).

In the California Teachers cohort study, there was a statistically significant increase in risk of breast cancer associated with early initiation of smoking among postmenopausal women, but this was not quite statistically significant in

Cancer Epidemiol Biomarkers Prev 2007;16(3):620–2

Received 10/19/06; revised 11/22/06; accepted 1/2/07.

Grant support: NIH National Cancer Institute CA17054 and CA74847, California Breast Cancer Research Program of the University of California grant 4PB-0092, and NIH contract no. N01-PC-35139.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Note: The collection of cancer incidence data used in this publication was supported by the California Department of Health Services as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885. The ideas and opinions expressed herein are those of the authors, and no endorsement by the State of California, Department of Health Services is intended or should be inferred.

Requests for reprints: Giske Ursin, Department of Preventive Medicine, Keck School of Medicine, University of Southern California/Norris Comprehensive Cancer Center, Room 4407, 1441 Eastlake Avenue, Los Angeles, CA 90089. Phone: 323-865-0423; Fax: 323-865-0142. E-mail: gursin@usc.edu

doi:10.1158/1055-9965.EPI-06-0873

Table 1. Adjusted odds ratios for breast cancer associated with various smoking measures

Variable	Cases (n = 1,728)	Controls (n = 441)	Adjusted* odds ratio (95% confidence intervals)
Ever smoked 100 cigarettes?			
No	991	261	1.00
Yes	737	180	0.99 (0.78-1.25)
P, Wald χ^2			0.93
Smoking status			
Never smoked	991	261	1.00
Former smoker	451	112	1.04 (0.80-1.36)
Current smoker	286	68	0.89 (0.64-1.24)
P, Wald χ^2			0.68
Total years of cigarette use			
Never smoked	991	261	1.00
≤11 y	238	68	0.94 (0.68-1.30)
>11 to ≤20 y	216	56	0.93 (0.66-1.31)
>20 y	283	56	1.12 (0.79-1.59)
P_{trend}			0.74
Age started smoking			
Never smoked	991	261	1.00
>18 y	205	55	0.94 (0.66-1.33)
>15 to ≤18 y	302	61	1.20 (0.86-1.67)
≤15 y	230	64	0.83 (0.59-1.16)
P_{Trend}			0.68
Lifetime cigarettes/wk			
Never smoked	991	261	1.00
≤8 cigarettes/wk	198	58	0.87 (0.62-1.23)
>8 to ≤52 cigarettes/wk	270	62	1.06 (0.76-1.47)
>52 cigarettes/wk	269	60	1.03 (0.73-1.45)
P_{Trend}			0.79
Cigarettes/wk in the last 5 y			
Never smoked	991	261	1.00
≤14 cigarettes/wk	101	33	0.71 (0.46-1.11)
>14 to ≤80 cigarettes/wk	145	32	0.95 (0.61-1.46)
>80 cigarettes/wk	152	31	1.09 (0.70-1.70)
Quit smoking >5 y ago	339	84	1.08 (0.80-1.44)
P_{Trend}†			0.78
Cigarettes/wk in a 5-y period after menarche			
Never smoked	991	261	1.00
≤8 cigarettes/wk	169	34	1.15 (0.76-1.74)
>8 to ≤28 cigarettes/wk	126	36	0.87 (0.57-1.33)
>28 cigarettes/wk	91	30	0.82 (0.51-1.31)
Did not smoke during this 5-y period	351	80	1.03 (0.76-1.39)
P_{Trend}‡			0.45
Cigarettes/wk from age 10 to 18 y			
Never smoked	991	261	1.00
≤5 cigarettes/wk	176	33	1.24 (0.81-1.88)
>5 to ≤13 cigarettes/wk	123	40	0.72 (0.48-1.09)
>13 cigarettes/wk	138	35	0.95 (0.62-1.44)
Did not smoke before age 18 y	300	72	1.04 (0.76-1.42)
P_{Trend}§			0.58
Smoked 1 y before age at first birth‖			
Never smoked	676	194	1.00
Did not smoke during year before first birth	174	57	0.92 (0.64-1.32)
Smoked during year before first birth	309	65	1.27 (0.90-1.79)
P, Wald χ^2			0.28
Amount smoked 1 y before first birth‖			
Never smoked	676	194	1.00
Did not smoke 1 y before first birth	174	57	0.92 (0.64-1.31)
≤70 cigarettes/wk	217	42	1.35 (0.90-2.00)
>70 cigarettes/wk	92	23	1.12 (0.67-1.89)
P, Wald χ^2			0.41
Years of smoking before first full-term pregnancy			
Never smoked	993	261	1.00
Smoked after first birth	50	12	0.97 (0.48-1.95)
≤10 y	350	92	0.95 (0.71-1.27)
>10 y	337	76	1.03 (0.75-1.43)
P, Wald χ^2			0.98

*Adjusted for age, race, education, age at menarche, age at first full-term pregnancy, parity, average drinks per week in recent 5 y, and family history of breast or ovarian cancer.
†Smokers who quit >5 y ago were excluded in the analysis for trend.
‡Smokers who did not smoke during the 5-y period after menarche were excluded in the analysis for trend.
§Smokers who did not smoke before age 18 y were excluded in the analysis for trend.
‖Nulliparous women were excluded from the analysis.

premenopausal/perimenopausal women (8). The Nurses' Health Studies I (9) and II (7) found statistically significant associations and/or trends with breast cancer risk among women who initiated smoking at an early age or smoked before their first pregnancy. A Norwegian-Swedish cohort study also found an increase associated with early initiation (10).

Our study strengths include the large sample size of young incident breast cancer cases and the in-person interviews

conducted with a structured questionnaire to collect detailed information on smoking and potential confounders. Our study had sufficient power to detect moderate positive associations if they existed, thus our power was similar to previously published studies (4, 12, 13).

A weakness in our study is the potential for survival bias. However, there was no indication that associations differed by stage, suggesting that survival bias is unlikely to have caused these findings.

Another disadvantage of this study is the potential for recall bias. We asked women to recall smoking patterns over decades of use. Although a clear association between smoking and breast cancer risk has not been established, women in the United States are inclined to believe that smoking is an important risk factor for breast cancer (24, 25). Women diagnosed with breast cancer would be expected to overestimate their past cigarette use compared with the control subjects. This would probably have resulted in a bias away from the null, generating an inflated risk, and is therefore unlikely to have been a problem in our case-control comparison.

In conclusion, our study does not support an effect of smoking at a young age on breast cancer risk among women under 50 years.

Acknowledgments

We thank the interviewers of this study and Juliana Bamrick for supervising the data collection.

References

1. Lash TL, Aschengrau A. Active and passive cigarette smoking and the occurrence of breast cancer. Am J Epidemiol 1999;149:5–12.
2. Band PR, Le ND, Fang R, Deschamps M. Carcinogenic and endocrine disrupting effects of cigarette smoke and risk of breast cancer. Lancet 2002; 360:1044–9.
3. Adami HO, Lund E, Bergstrom R, Meirik O. Cigarette smoking, alcohol consumption, and risk of breast cancer in young women. Br J Cancer 1988; 58:832–7.
4. Smith SJ, Deacon JM, Chilvers CED; Group UNC-CS. Alcohol, smoking, passive smoking, and caffeine in relation to breast cancer risk in young women. Br J Cancer 1994;70:112–9.
5. Gammon MD, Schoenberg JB, Teitelbaum SL, et al. Cigarette smoking and breast cancer risk among young women (United States). Cancer Causes Control 1998;9:583–90.
6. Marcus PM, Newman B, Millikan RC, Moorman PG, Baird DD, Qaqish B. The associations of adolescent cigarette smoking, alcoholic beverage consumption, environmental tobacco smoke, and ionizing radiation with subsequent breast cancer risk (United States). Cancer Causes Control 2000; 11:271–8.
7. Al-Delaimy WK, Cho E, Chen WY, Colditz G, Willet WC. A prospective study of smoking and risk of breast cancer in young adult women. Cancer Epidemiol Biomarkers Prev 2004;13:398–404.
8. Reynolds P, Hurley S, Goldberg DE, et al. Active smoking, household passive smoking, and breast cancer: evidence from the California Teachers Study. J Natl Cancer Inst 2004;96:29–37.
9. Egan KM, Stampfer MJ, Hunter D, et al. Active and passive smoking in breast cancer: prospective results from the Nurses' Health Study. Epidemiology 2002;13:138–45.
10. Gram IT, Braaten T, Terry PD, et al. Breast cancer risk among women who start smoking as teenagers. Cancer Epidemiol Biomarkers Prev 2005; 14:61–6.
11. Innes KE, Byers TE. Smoking during pregnancy and breast cancer risk in very young women. Cancer Causes Control 2001;12:179–85.
12. Johnson KC, Hu J, Mao Y; Group TCCRER. Passive and active smoking and breast cancer risk in Canada, 1994–97. Cancer Causes Control 2000; 11:211–21.
13. Kropp S, Chang-Claude J. Active and passive smoking and risk of breast cancer by age 50 years among German women. Am J Epidemiol 2002;156: 616–26.
14. Chu SY, Stroup NE, Wingo PA, Lee NC, Peterson HB, Gwinn ML. Cigarette smoking and the risk of breast cancer. Am J Epidemiol 1990;131: 244–53.
15. Ma H, Bernstein L, Ross RK, Ursin G. Hormone-related risk factors for breast cancer in women under age 50 years by estrogen and progesterone receptor status: results from a case-control and a case-case comparison. Breast Cancer Res 2006;8:R39.
16. McTiernan A, Thomas DB, Johnson LK, Roseman D. Risk factors for estrogen receptor-rich and estrogen receptor-poor breast cancers. J Natl Cancer Inst 1986;77:849–54.
17. Haile RW, Witte JS, Ursin G, et al. A case-control study of reproductive variables, alcohol, and smoking in premenopausal bilateral breast cancer. Breast Cancer Res Treat 1996;37:49–56.
18. Stanford JL, Szklo M, Boring CC, et al. A case-control study of breast cancer stratified by estrogen receptor status. Am J Epidemiol 1987;125: 184–94.
19. Smith EM, Sowers MF, Burns TL. Effects of smoking on the development of female reproductive cancers. J Natl Cancer Inst 1984;73:371–6.
20. Schechter MT, Miller AB, Howe GR, Baines CJ, Craib KJ, Wall C. Cigarette smoking and breast cancer: case-control studies of prevalent and incident cancer in the Canadian National Breast Screening Study. Am J Epidemiol 1989;130:213–20.
21. Manjer J, Berglund G, Bondesson L, Garne JP, Janzon L, Malina J. Breast cancer incidence in relation to smoking cessation. Breast Cancer Res Treat 2000;61:121–9.
22. IARC. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Tobacco smoke and involuntary smoking. Volume 83. Lyon: IARC Press; 2004.
23. Hamajima N, Hirose K, Tajima K, et al. Alcohol, tobacco, and breast cancer—collaborative reanalysis of individual data from 53 epidemiological studies, including 58515 women with breast cancer and 95067 women without the disease. Br J Cancer 2002;87:1234–45.
24. Silverman E, Woloshin S, Schwartz LM, Byram SJ, Welch HG, Fischhoff B. Women's views on breast cancer risk and screening mammography: a qualitative interview study. Med Decis Making 2001;21:231–40.
25. Wold KS, Byers T, Crane LA, Ahnen D. What do cancer survivors believe causes cancer? (United States). Cancer Causes Control 2005;16:115–23.

Cigarette Smoking Is Not Associated with Breast Cancer Risk in Young Women

Jennifer Prescott, Huiyan Ma, Leslie Bernstein, et al.

Cancer Epidemiol Biomarkers Prev 2007;16:620-622.