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Null Results in Brief

Cancer Epidemiology, Biomarkers & Prevention

Environmental Tobacco Smoke Exposure and Survival Following Breast Cancer

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Abstract

Background: Environmental tobacco smoke (ETS) exposure is hypothesized to influence survival after breast cancer, but few studies have examined this association.

Methods: A population-based cohort of women ($N = 1,508$) diagnosed with first primary invasive or *in situ* breast cancer in 1996 to 1997 was interviewed shortly after diagnosis and again approximately 5 years later to assess ETS exposure, and women were followed for more than 18 years using the National Death Index; 597 deaths (237 associated with breast cancer) were identified. Multivariable Cox regression was used to estimate adjusted HRs and 95% confidence intervals (CI) for mortality among women with breast cancer as related to at-diagnosis and at-/postdiagnosis changes in ETS exposure.

Results: There was little or no association between at-diagnosis ETS exposure and all-cause (HR = 1.04; 95% CI, 0.78–1.40) or breast cancer–specific (HR = 0.98; 95% CI, 0.63–1.52) mortality. Mortality was elevated among women who reported cessation in postdiagnosis ETS exposure up to 1 year before the follow-up assessment, for all-cause (HR = 1.81; 95% CI, 0.87–3.74) and breast cancer mortality (HR = 1.89; 95% CI, 0.68–5.24); however, estimates were imprecise.

Conclusions: We found little evidence of an association between at-diagnosis ETS exposure and mortality after breast cancer. Postdiagnosis cessation of ETS exposure was positively associated with mortality, although we could not rule out chance and reverse causation as possible explanations.

Impact: Exposure to ETS does not appear to influence mortality after breast cancer. *Cancer Epidemiol Biomarkers Prev; 26(2); 278–80. ©2016 AACR.*

Introduction

Few studies (1–4) have examined whether environmental tobacco smoke (ETS) exposure increases the risk of mortality among women with breast cancer, and no studies to date have prospectively examined the impact of postdiagnosis changes in ETS exposure on mortality. This study examined whether ETS exposure was associated with long-term all-cause and breast cancer–specific mortality among a population-based sample of women.

Materials and Methods

Participants of the Long Island Breast Cancer Study Project (LIBCSP), a population-based cohort of women newly diagnosed with breast cancer, were interviewed shortly after diagnosis and again about 5 years later and now continue to be followed for vital status. Details of the LIBCSP have been published previously (2, 5). Institutional Review Board approval was obtained from of all participating institutions.

ETS exposure assessment

ETS exposure was determined via structured interviews (2). Women were asked to report whether any members of the household smoked in their presence, the relationship of the smoker, the participant's ages at first/last exposure, and any time periods the household member did not smoke. Duration of exposure was categorized as <15 years, ≥15 to <30 years, and ≥30 years of exposure. Recency of exposure was categorized as <5 years, ≥5 to <10 years, and ≥10 years.

Covariate assessment

Covariates assessed via questionnaire included age, menopausal status, annual household income, education, marital status, body mass index (BMI), physical activity, intake of alcoholic beverages, cigarette smoking, and treatment. Estrogen receptor status and nodal involvement were determined by medical record. Tumor size was obtained from the NY State Cancer Registry.

Outcome assessment

Vital status of the 1,508 women diagnosed with breast cancer was determined using the National Death Index. Follow-up for

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Table 1. Cox regression HRs and 95% CIs for the association between prediagnosis and at-diagnosis ETS exposure and mortality in the LIBCSP women diagnosed with breast cancer in 1996–1997 ($N = 1{,}508$)

	All-cause mortality (deaths, $n = 597$)				Breast cancer–specific mortality (deaths, $n = 237$)			
ETS exposure At-diagnosis	**Deaths**	**Censored**	**Age adjusted HR (95% CI)**	**Multivariable adjusted[a] HR (95% CI)**	**Deaths**	**Censored**	**Age adjusted HR (95% CI)**	**Multivariable adjusted[a] HR (95% CI)**
ETS exposure status[b]								
Never	119	176	1 (Ref.)	1 (Ref.)	49	246	1 (Ref.)	1 (Ref.)
Former	376	585	1.00 (0.81–1.23)	0.98 (0.80–1.22)	141	820	0.87 (0.63–1.21)	0.89 (0.64–1.24)
Current	84	138	1.25 (0.94–1.66)	1.04 (0.78–1.40)	38	184	1.04 (0.68–1.59)	0.98 (0.63–1.52)
Duration of ETS exposure								
Never	119	176	1 (Ref.)	1 (Ref.)	49	246	1 (Ref.)	1 (Ref.)
Former								
<15 years	50	91	1.05 (0.75–1.46)	1.13 (0.80–1.59)	24	117	1.02 (0.62–1.66)	1.10 (0.67–1.81)
≥15–<30 years	131	289	0.89 (0.69–1.14)	0.90 (0.69–1.16)	60	360	0.84 (0.57–1.23)	0.84 (0.57–1.24)
≥30 years	175	187	1.06 (0.84–1.34)	1.00 (0.79–1.28)	54	308	0.90 (0.61–1.33)	0.89 (0.60–1.33)
Current								
<15 years	7	7	1.74 (0.81–3.73)	1.52 (0.70–3.27)	<5	12	—	—
≥15–<30 years	13	22	1.59 (0.89–2.84)	1.32 (0.74–2.36)	6	29	1.08 (0.46–2.55)	0.97 (0.41–2.29)
≥30 years	62	106	1.14 (0.83–1.55)	0.93 (0.67–1.29)	30	138	1.07 (0.68–1.69)	1.01 (0.63–1.61)
ETS exposure recency								
Never	119	176	1 (Ref.)	1 (Ref.)	49	246	1 (Ref.)	1 (Ref.)
Former								
<5 years	26	41	1.05 (0.69–1.60)	0.95 (0.62–1.47)	12	55	1.07 (0.57–2.01)	0.99 (0.52–1.87)
≥5–<10 years	47	69	1.07 (0.77–1.51)	1.00 (0.71–1.41)	16	100	0.82 (0.47–1.45)	0.76 (0.43–1.35)
≥10 years	303	475	0.99 (0.80–1.22)	0.99 (0.79–123)	113	665	0.86 (0.62–1.21)	0.90 (0.64–1.27)
Current	84	138	1.25 (0.94–1.66)	1.04 (0.78–1.40)	38	184	1.04 (0.68–1.59)	0.98 (0.63–1.53)

NOTE: LIBCSP participants diagnosed with breast cancer between August 1, 1996, and July 31, 1997, followed-up for vital status through December 31, 2014.
[a]Adjusted for age at diagnosis, BMI, marital status, income, alcohol intake, physical activity, and active cigarette smoking status.
[b]ETS exposure status was defined as never, former, and current exposure to tobacco smoke from any household members.

mortality occurred from the date of diagnosis in 1996 to 1997 until December 31, 2014 (median = 17.61 years). We identified 597 deaths; 234 were associated with breast cancer.

Statistical analysis

Using multivariable Cox proportional regression models, we estimated HR and 95% confidence intervals (CI) for the associations between at-diagnosis as well as at-/postdiagnosis changes in ETS exposure and mortality following breast cancer. Models restricted to women with invasive cancer only yielded similar results from those of all women; only the latter are shown. All analyses were conducted using IBM SPSS Statistics Version 22.0 (IBM Corp.).

In analyses of at-diagnosis ETS exposure, survival time began at the date of breast cancer diagnosis and ended on the date of death or, if alive, December 31, 2014. In analyses examining postdiagnosis ETS exposure, survival time began at the date of completion of the follow-up questionnaire and ended on the date of death or, if alive, December 31, 2014. Missing covariates were imputed in SPSS using 25 imputations with 1,000 iterations. The imputation models included age at diagnosis, menopausal status, income, education, marital status, BMI, physical activity, alcohol intake, smoking status, post-diagnosis ETS exposure, disease characteristics (stage, tumor size, nodal involvement estrogen receptor status), treatment (radiation, chemotherapy, and hormone therapies), and the outcome (the event indicator and the Nelson–Aalen cumulative hazard estimator).

Results

Approximately 15% of women reported ETS exposure in the year before diagnosis and 14% reported current exposure at the follow-up questionnaire.

At-diagnosis ETS exposure

There was little or no association between current ETS exposure and all-cause (HR = 1.04; 95% CI, 0.78–1.40) or breast cancer–specific (HR = 0.98; 95% CI, 0.63–1.52) mortality after adjustment for covariates (Table 1). Risk of mortality was slightly elevated for all-cause (HR = 1.17; 95% CI, 0.74–1.86) and breast cancer–specific (HR = 1.13; 95% CI, 0.57–2.27) mortality when we restricted the analyses to never smokers, although the corresponding estimates were imprecise.

At-/postdiagnosis ETS exposure

Although no associations were observed among women with ongoing ETS exposure, HRs were elevated 81% (HR = 1.81; 95% CI, 0.87–3.74) for all-cause mortality and 89% (HR = 1.89; 95% CI, 0.68–5.24) for breast cancer–specific mortality among women who reported cessation in postdiagnosis ETS exposure up to the year before the follow-up assessment (Table 2).

Discussion

Exposure to the constituents of tobacco smoke, either through active smoking or exposure to ETS, is hypothesized to influence breast cancer progression through several mechanisms, including directly by influencing cell proliferation and metastasis (6) and indirectly by disrupting the endocrine system (7). In addition, because up to 70% of tar in ETS is in the vapor phase, whereas all of the tar in direct smoking is in the particulate phase, ETS may be an important source of exposure to carcinogens as particulate smoke is cleared into the mouth and swallowed, but vapor phase constituents are inhaled and absorbed into the bloodstream and lymph system (8). Despite these hypothesized mechanisms, the few studies conducted to date (1–4), including the sufficiently powered study reported here, provide limited or no evidence of an

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Table 2. Cox regression HRs and 95% CIs for the association between at-/postdiagnosis ETS exposure and mortality in the LIBCSP women diagnosed with breast cancer in 1996–1997 ($N = 1{,}339$).

	All-cause mortality (deaths, $n = 428$)				Breast cancer–specific mortality (deaths, $n = 126$)			
ETS exposure			**Age adjusted**	**Multivariable adjusted[a]**			**Age adjusted**	**Multivariable adjusted[a]**
At-diagnosis/postdiagnosis	**Deaths**	**Censored**	**HR (95% CI)**	**HR (95% CI)**	**Deaths**	**Censored**	**HR (95% CI)**	**HR (95% CI)**
ETS exposure status								
Never/Never	79	163	1 (Ref.)	1 (Ref.)	23	219	1 (Ref.)	1 (Ref.)
Never/Former	10	18	1.14 (0.44–2.94)	0.94 (0.35–2.58)	<5	24	–	–
Former/Never	251	529	1.03 (0.79–1.35)	1.03 (0.78–1.36)	69	711	0.93 (0.56–1.54)	0.92 (0.55–1.54)
Former/Former	5	14	0.96 (0.21–4.54)	0.72 (0.14–3.58)	<5	18	–	–
Former/Current	21	48	1.32 (0.72–2.43)	1.05 (0.56–1.99)	8	61	1.16 (0.43–3.18)	0.87 (0.31–2.46)
Current/Never	22	43	1.29 (0.76–2.20)	1.19 (0.67–2.09)	6	58	1.00 (0.38–2.63)	0.88 (0.32–2.42)
Current/Former	14	18	1.99 (0.97–4.09)	1.81 (0.87–3.74)	6	26	2.20 (0.81–5.97)	1.89 (0.68–5.24)
Current/Current	26	78	1.18 (0.70–1.99)	1.02 (0.59–1.77)	8	96	0.82 (0.33–2.06)	0.66 (0.24–1.81)

NOTE: LIBCSP participants diagnosed with breast cancer between August 1, 1996, and July 31, 1997, followed-up for vital status through December 31, 2014. Complete-case analyses exclude women who died within 5 years of breast cancer diagnosis ($n = 169$).

[a]Adjusted for age at diagnosis, BMI, marital status, income, alcohol intake, physical activity, stage, tumor size, nodal involvement, estrogen receptor status, chemotherapy treatment, and postdiagnosis active cigarette smoking status.

association between ETS exposure and survival after breast cancer. Although we observed an elevated risk of mortality among women with postdiagnosis cessation of ETS exposure, we could not rule out chance and reverse causation as possible explanations.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): P.T. Bradshaw, S.L. Teitelbaum, A.I. Neugut, R.M. Santella, M.D. Gammon

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Study supervision: M.D. Gammon

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