Dietary Fats and All-cause and Breast Cancer–specific Mortality among Women with Breast Cancer: The Western New York Exposures and Breast Cancer Study

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ABSTRACT

Background: Study results of prediagnostic dietary fat intake and breast cancer mortality have been inconclusive. While dietary fat subtypes [saturated (SFA), polyunsaturated (PUFA), and monounsaturated (MUFA) fatty acids] may have different biological effects, there is little evidence regarding the association of dietary fat and fat subtype intake with mortality after breast cancer diagnosis.

Methods: Women with incident, pathologically confirmed invasive breast cancer and complete dietary data (n = 793) were followed in a population-based study, the Western New York Exposures and Breast Cancer study. Usual intake before diagnosis of total fat and subtypes were estimated from a food frequency questionnaire completed at baseline. HRs and 95% confidence intervals (CI) for all-cause and breast cancer–specific mortality were estimated with Cox proportional hazards models. Interactions by menopausal status, estrogen receptor (ER) status, and tumor stage were examined.

Results: Median follow-up time was 18.75 years; 327 (41.2%) participants had died. Compared with lower intake, greater intake of total fat (HR, 1.05; 95% CI, 0.65–1.70), SFA (1.31; 0.82–2.10), MUFA (0.99; 0.61–1.60), and PUFA (0.99; 0.56–1.75) was not associated with breast cancer–specific mortality. There was also no association with all-cause mortality. Results did not vary by menopausal status, ER status, or tumor stage.

Conclusions: Prediagnostic intake of dietary fat and fat subtypes was not associated with either all-cause or breast cancer mortality in a population-based cohort of breast cancer survivors.

Impact: Understanding factors affecting survival among women diagnosed with breast cancer is critically important. Dietary fat intake prior to diagnosis may not impact that survival.

Introduction

Results of studies of prediagnostic dietary fat intake in association with mortality from breast cancer have been inconclusive. In a systematic review of diet and breast cancer survival, associations of prediagnostic intake of total and saturated fat with all-cause mortality were classified as "limited-suggestive" (1). While dietary fat subtypes [saturated (SFA), polyunsaturated (PUFA), and monounsaturated (MUFA) fatty acids] may have different biological effects (2, 3), there are few studies examining fat subtypes with breast cancer mortality (4–6). We report here on the association of prediagnostic, self-reported dietary intake of total fat and fat subtypes with breast cancer-specific and all-cause mortality among women with breast cancer in a population-based study.

Materials and Methods

Included in this prospective analysis were women with primary, incident, pathologically confirmed breast cancer and complete dietary data, cases from the Western New York Exposures and Breast Cancer (WEB) study, a population-based case–control study (7). Participants with stage 4 disease (n = 37) were excluded. Follow-up for breast cancer–specific and all-cause mortality was through the National Death Index until December 31, 2018. Survival time was calculated as time from date of diagnosis until date of death or December 31, 2018, whichever came first. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. Written informed consent was obtained from all participants; the study was approved by the Institutional Review Boards of the University at Buffalo, State University of New York, and participating hospitals.

Usual prediagnostic intake of total fat and fat subtypes were estimated from a food frequency questionnaire completed at baseline for 12–24 months prior to diagnosis (7). Dietary fat intake measures were adjusted for total energy, calculated as percent of total calories. HRs and 95% confidence intervals (CI) were estimated using Cox proportional hazards models for tertiles of intake of percent of kilocalories from total fat and fat subtypes (SFA, MUFA, and PUFA) in relation to all-cause and breast cancer–specific mortality. Covariates, selected *a priori* based on existing research, were included in the final model if addition changed HRs by 10% or more for a model including age and kilocalories. Final models were adjusted for age, tumor stage, ER status, education, body mass index (BMI), race/ethnicity, menopausal status, and smoking status (current, former, never). Tumor grade was not included in this analysis. Additional analyses included examination of interaction by menopausal status and ER status and models stratified by tumor stage (stage I, II, and III).

Data availability

The deidentified data for these analyses can be shared on the basis of reasonable requests to the corresponding author upon approval by the WEB study research committee.

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Results

Median follow-up time was 18.75 years. Among 793 women with invasive breast cancer, 327 (41.2%) had died. Characteristics associated with mortality in this study population have been reported previously (8). Comparisons of participant characteristics by fat intake among those alive and deceased at the end of the follow-up are shown in **Table 1**. Among the deceased, those with higher compared with lower fat intake had had more births. Among those still alive, age, age at menopause, years of education, weight, and BMI were different by fat intake without a consistent direction of association.

In adjusted models, total dietary fat and fat subtypes were not associated with survival (**Table 2**). There was no evidence of interaction by menopausal status or ER status. Furthermore, there were no associations between risk of mortality and dietary fat intake within strata of stage.

Table 1. Descriptive characteristics of the breast cancer cases by tertile of total dietary fat intake and by vital status, WEB study.

	Deceased $n = 327$				Alive $n = 466$			
	Tertile 1 (<33% of daily total kcal from fat)	Tertile 2 (≥33–39% of daily total kcal from fat)	Tertile 3 (≥39% of daily total kcal from fat)	P_{TREND}	Tertile 1 (<33% of daily total kcal from fat)	Tertile 2 (≥33–39% of daily total kcal from fat)	Tertile 3 (≥39% of daily total kcal from fat)	P_{TREND}
Mean (SD)								
Age, years	62.4 (11.4)	61.2 (10.8)	61.9 (11.6)	0.73	55. 1 (9.0)	54.6 (9.9)	52.2 (9.7)	0.02
Age at menarche, years	12.4 (1.6)	12.7 (1.7)	12.7 (1.6)	0.55	12.6 (1.6)	12.6 (1.6)	12.6 (1.6)	0.93
Age at first birth, years	24.9 (4.9)	24.2 (4.8)	23.4 (5.0)	0.13	24.6 (4.8)	24.8 (4.7)	23.8 (5.3)	0.25
Age at menopause, years	48.0 (5.5)	48.7 (6.0)	47.7 (5.4)	0.44	48.7 (5.2)	49.2 (4.2)	47.0 (5.9)	0.01
Number of births	2.0 (1.5)	2.8 (1.8)	2.7 (2.2)	0.01	2.2 (1.5)	2.1 (1.5)	2.2 (1.5)	0.93
Education, years	13.1 (3.0)	13.1 (2.5)	12.5 (2.6)	0.11	14.2 (2.5)	14.0 (2.4)	13.5 (2.6)	0.02
Mean (SD)								
Weight, *kg*	78.7 (19.6)	79.0 (17.4)	76.2 (16.7)	0.43	70.5 (14.2)	76.4 (19.4)	77.8 (17.6)	0.003
Height, *cm*	161.9 (6.7)	162.1 (7.1)	160.8 (7.1)	0.31	163.2 (6.2)	163.9 (5.9)	163.0 (5.9)	0.39
BMI	30.1 (7.4)	30.1 (6.3)	29.5 (6.3)	0.78	26.6 (5.3)	28.5 (7.1)	29.2 (6.2)	0.00
Mean (SD)								
Kilocalories (daily)	1293.7 (445.7)	1534.7 (561.5)	1706.4 (832.4)		1371.4 (424.9)	1524.3 (529.9)	1814.5 (740.6)	
Total fat *g*	40.0 (16.1)	62.3 (24.1)	85.6 (42.9)		41.5 (15.8)	61.3 (22.7)	91.1 (37.9)	
Saturated fat *g*	14.2 (6.3)	22.4 (9.2)	31.3 (16.9)		14.9 (6.3)	22.4 (8.8)	33.0 (14.6)	
Monounsaturated fat *g*	14.2 (6.0)	22.9 (9.1)	31.8 (16.2)		14.9 (6.1)	22.5 (8.6)	14.4 (9.6)	
Polyunsaturated fat *g*	6.6 (3.6)	10.5 (4.8)	14.4 (7.9)		6.6 (3.1)	4.8 (2.5)	8.0 (3.7)	
Race/Ethnicity *n (%)*				0.18				0.12
Caucasian	80 (92.0)	111 (92.5)	103 (85.8)		163 (96.5)	156 (97.5)	116 (84.7)	
All others	7 (8.0)	9 (7.5)	17 (14.2)		6 (3.5)	4 (2.5)	21 (15.3)	
Smoking status *n (%)*				0.18				
Never	42 (48.3)	46 (38.3)	68 (49.6)		83 (49.1)	65 (40.6)	52 (43.3)	0.77
Former	38 (43.7)	51 (42.5)	41 (29.9)		75 (44.4)	83 (51.9)	46 (38.3)	
Current	7 (8.1)	23 (19.2)	28 (20.4)		11 (6.5)	11 (6.9)	22 (18.3)	
Menopausal status *n (%)*				0.98				0.07
Premenopausal	15 (17.2)	22 (18.3)	21 (17.5)		50 (29.6)	58 (36.3)	58 (42.3)	
Postmenopausal	72 (82.8)	98 (81.7)	99 (82.5)		119 (70.4)	102 (63.7)	79 (57.7)	
Family history of breast cancer *n (%)*								
Yes	64 (73.6)	89 (74.2)	88 (73.3)	0.65	116 (68.6)	122 (76.3)	101 (72.7)	0.43
No	20 (23.0)	23 (19.2)	22 (18.3)		40 (23.7)	31 (19.4)	25 (18.3)	
Unknown	3 (3.5)	8 (6.7)	10 (8.3)		13 (7.7)	7 (4.4)	11 (8.0)	
Estrogen receptor status *n (%)*				0.75				0.27
Negative	24 (27.6)	32 (26.7)	33 (24.1)		5 (32.5)	47 (29.4)	29 (24.2)	
Positive	58 (66.7)	82 (68.3)	102 (74.5)		112 (66.3)	111 (69.4)	88 (73.3)	
Unknown/Not done	5 (5.8)	6 (5.0)	3 (2.5)		2 (1.2)	2 (1.3)	2 (1.5)	
Progesterone receptor status *n (%)*				0.99				0.84
Negative	50 (57.5)	44 (36.7)	46 (38.3)		54 (32.0)	56 (35.0)	44 (32.1)	
Positive	32 (36.8)	69 (57.5)	70 (68.3)		112 (66.3)	102 (63.7)	89 (65.0)	
Unknown/Not done	5 (5.8)	7 (5.8)	4 (3.3)		3 (1.8)	2 (1.3)	4 (2.9)	
Stage at diagnosis *n (%)*				0.26				0.12
I	43 (49.4)	60 (50.0)	68 (56.7)		118 (69.8)	102 (63.8)	76 (55.5)	
II	41 (47.1)	57 (47.5)	44 (36.7)		48 (28.4)	56 (35.0)	57 (41.6)	
III	3 (3.5)	3 (2.5)	8 (6.7)		3 (1.8)	2 (1.3)	4 (2.9)	

Note: Includes individuals self-identified as American Indian or Alaskan Native, Asian or Pacific Islander (Chinese, Indo-Chinese, Korean, Japanese, Pacific Islander, Vietnamese, Black of African American, Hispanic/Latino (Mexican, Cuban, Puerto Rican, Central American or South American, or Other as specified.

Table 2. Adjusted HRs and 95% CIs for the association between dietary fat type intake and death from all causes and death from breast cancer the WEB study.

		All causes	Breast cancer
Total fat (% of total daily kcals from fat)[a]			
T1	<33%	*ref*	*ref*
T2	≥33%–39%	1.23 (0.93–1.65)	1.03 (0.65–1.63)
T3	≥39%	1.27 (0.94–1.73)	1.05 (0.65–1.70)
P_{TREND}		0.26	0.87
Saturated fat (%of total daily kcals from saturated fat)[a]			
T1	<11%	*ref*	*ref*
T2	≥11%–14.5%	1.25 (0.94–1.65)	1.17 (0.72–1.89)
T3	≥14.5%	1.12 (0.83–1.50)	1.31 (0.82–2.10)
P_{TREND}		0.34	0.25
MUFA (% of total daily fat kcals from MUFA)[a]			
T1	<35%	*ref*	*ref*
T2	≥35%–38%	1.31 (0.99–1.74)	1.61 (1.03–2.53)
T3	≥38%	1.10 (0.82–1.47)	0.99 (0.61–1.60)
P_{TREND}		0.69	0.51
PUFA (% of total daily fat kcals from PUFA)[a]			
T1	<14%	*ref*	*ref*
T2	≥14%–18%	0.91 (0.68–1.21)	1.22 (0.71–2.12)
T3	≥18%	1.23 (0.94–1.60)	0.99 (0.56–1.75)
P_{TREND}		0.19	0.55

Abbreviations: MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.
[a]Models are adjusted for age, BMI, years of education, race/ethnicity, menopausal status, smoking status, breast cancer stage, and ER status.

Discussion

Examination of dietary fat subtypes in additional to total dietary fat intakes potentially could explain inconsistent results regarding associations of dietary fat with breast cancer mortality. Fatty acids are hypothesized to influence carcinogenesis because of effects on circulating estrogen, oxidative stress, and inflammation (2, 3); differences in effects by fat subtypes are less clear (3). High- and low-fat diets may differ in the proportion of fat subtypes as well as in the dietary source of the fat. In a secondary data analysis of the Women's Health Initiative dietary intervention trial, participants following the low-fat eating pattern had lower mortality after breast cancer; it was not clear, however, whether the effect resulted from the fat intake or to other, associated changes in diet such as changed consumption of fruits and vegetables or animal products (9).

We found no association of prediagnostic intake of total fat or SFA, with either all-cause or breast cancer–specific mortality, consistent with some, but not all, studies of prediagnostic total dietary fat (1, 5). We found no associations of either MUFA or PUFA intake with risk of all-cause or breast cancer–specific mortality, consistent with most recent studies (6).

Strengths of this study include the study sample of population-based, incident, histologically confirmed breast cancer cases, the length of follow-up, and the use of validated tools for diet assessment. Limitations include the potential for residual confounding which may persist despite efforts to control it. Our analysis was limited to a report of usual prediagnostic intake, which likely includes nondifferential misclassification. Furthermore, the measured timepoint might not be the critical window for exposure relative to survival. In addition, we could not account for change, if any, in diet following diagnosis. Finally, other dietary components such as the source of dietary fat and total energy intake may also impact survival; we adjusted for energy intake but not other factors.

In our cohort, intake of dietary fat and its subtypes were not associated with mortality among women with breast cancer.

Authors' Disclosures

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Authors' Contributions

D.S. Meyer: Formal analysis, writing–original draft. **A.E. Millen:** Writing–review and editing. **J. Nie:** Data curation, formal analysis, writing–review and editing. **M. Trevisan:** Writing–review and editing. **J.L. Freudenheim:** Conceptualization, supervision, funding acquisition, methodology, writing–review and editing.

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