Dietary patterns and breast density in the Minnesota Breast Cancer Family Study

Marilyn Tseng · Robert A. Vierkant · Lawrence H. Kushi · Thomas A. Sellers · Celine M. Vachon

Abstract
Objective Whether dietary patterns, rather than single foods or nutrients, are associated with breast density is not known. We investigated this in the Minnesota Breast Cancer Family Study.
Methods Participants completed a 153-item food frequency questionnaire and provided screening mammograms for breast density assessment using a computer-assisted method. We used multivariate linear regression to quantify dietary pattern–breast density associations.
Results Among 3,147 women with dietary information, three dietary patterns emerged from principal components analysis: a fruit–vegetable–cereal pattern, a salad–sauce–pasta/grain pattern, and a meat–starch pattern. Among 1,286 women with breast density estimates, the fruit–vegetable–cereal and salad–sauce–pasta/grain patterns were inversely associated with percent breast density only in stratified analyses. The fruit–vegetable–cereal pattern was inversely associated with breast density among premenopausal women (β = -0.13, p = 0.09; interaction p = 0.009) and current smokers, (β = -0.30, p = 0.02; interaction p = 0.05), while the salad–sauce–pasta/grain was inversely associated with breast density among current smokers (β = -0.27, p = 0.06; interaction p = 0.006).
Conclusion Overall our results do not provide strong evidence for associations of dietary patterns with breast density. Suggestive inverse associations for the fruit–vegetable–cereal and salad–sauce–pasta/grain dietary patterns among smokers are consistent with previous reports and leave open the possibility that some dietary patterns influence breast density in population subsets. Nevertheless, these findings require confirmation, and their underlying reasons have yet to be clarified.

Keywords Breast neoplasms · Diet · Dietary patterns · Mammographic density

M. Tseng
Division of Population Science, Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111, USA

R. A. Vierkant
Division of Biostatistics, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN, USA

L. H. Kushi
Division of Research, Kaiser Permanente, Oakland, CA, USA

T. A. Sellers
Division of Cancer Prevention and Control, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

C. M. Vachon
Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN, USA

Introduction

Despite continued interest in diet modification for breast cancer prevention, epidemiologic studies have not consistently implicated specific dietary factors. Most previous studies have examined single factors or components of the diet. Only a small number of studies [1–7] have addressed a broader question of whether overall diet or dietary patterns, rather than individual dietary components, affect breast cancer risk.

Breast density, the percentage of total breast area with a mammographically dense appearance, is a useful surrogate marker for breast cancer risk in epidemiologic studies [8].

It is strongly associated with breast cancer risk [9, 10], is modifiable [11–13], and changes in this factor have recently been associated with changes in risk [14]. Although individual dietary components have been examined with breast density, only one study has examined the association of dietary patterns with breast density [15]. The objectives of this analysis were to characterize dietary patterns among women enrolled in the Minnesota Breast Cancer Family Study, and to examine associations of these dietary patterns with breast density.

Materials and methods

Study sample

The study sample included participants in the Minnesota Breast Cancer Family Study [16]. The Minnesota Breast Cancer Family Study was initiated in 1990 as a follow-up to a 1944 family study that included 544 breast cancer probands ascertained at the Tumor Clinic of the University of Minnesota Hospital. Eligible participants for the follow-up study included sisters, daughters, nieces, and granddaughters of the original probands, and spouses of male first- and second-degree relatives. Upon enrollment, women completed telephone interviews and dietary questionnaires. Women at least 40 years of age were also asked to provide a recent mammogram.

Of 9,084 women in the original cohort, we excluded those who were interviewed through a surrogate ($N = 2{,}903$), who did not return a food frequency questionnaire (FFQ) ($N = 2{,}685$), who reported an infeasible caloric intake (<600 kcal/day or > 5,000 kcal/day) ($N = 224$), or who left at least 30 missing responses on the FFQ ($N = 125$), leaving 3,147 women available for analysis of dietary patterns. In analyses relating dietary patterns to breast density measures, we additionally excluded 1,710 women without mammographic images assessed for breast density and 53 women with a breast cancer diagnosis at enrollment into the follow-up study, leaving 1,384 women available for these analyses.

The project was approved by the Institutional Review Boards at the Mayo Clinic and the Fox Chase Cancer Center.

Data collection

Data collection methods for the study have been described previously [16, 17]. Briefly, telephone interviews were completed for all available female relatives 18 years and older. The collected data included history of cancer, marital status, education, menstrual and pregnancy history, oral contraceptive use, physical activity, and history of smoking and alcohol intake. Menopausal status was assessed by the response to a question of whether the participant had a menstrual period within the last year, excluding periods brought on by hormones. After the telephone interview, each subject additionally received in the mail a body measurement questionnaire designed to elicit measures of height, weight, and circumferences of the waist (2 inches above the umbilicus) and hip (maximal protrusion) [18]. To assess usual dietary intake over the past year, participants were asked to complete a 153-item semi-quantitative food frequency questionnaire adapted from Willett et al. [19], with frequency response options for each food item ranging from "never or less than once per month" to "six or more times per day."

Breast density assessment

Women aged 40 years or older were asked to provide a recent mammogram to verify their breast cancer status and to allow estimation of breast density. If no mammogram had been taken in the previous year (2 years if <50 years at time of interview), they were instructed to obtain a new one through their personal physician. Percent breast density was estimated using the semi-automated breast density method developed by Dr. Martin Yaffe and colleagues at the University of Toronto [20]. The method involves dividing the mammographic image into a distribution of gray values, then setting two thresholds: one that differentiates the edge of the breast from the rest of the mammogram, and the other that identifies the border of the region(s) in the pixel distribution representing the radiographically dense tissue in the image. Higher gray value pixels are thought to be a result of fibroglandular tissue, and lower gray values a result of fat tissue. Dividing the pixels related to fibroglandular tissue by the total number of pixels making up the entire breast allowed for an estimate of percent breast density. This measure has consistently been associated with breast cancer [21, 22], and has high intra-observer correlation (>0.95 for our reader on over 700 mediolateral oblique (MLO) and cranial-caudal (CC) images). Breast density assessments were available for 1,384 women: 1,169 with both MLO and CC views, 268 with MLO views only, and 27 with CC views only. Because we had density assessments for more MLO views than for CC views, we present results based on MLO views, but findings based on CC views in additional analyses were similar.

Identification of dietary patterns

Patterns of food intake were identified by principal components analysis (PCA) [23, 24] using frequency responses

to the dietary questionnaire. (An example of SAS programming statements used to run the analysis is provided at http://www.fccc.edu/research/labs/tseng/TsengDOD01.html.) Individuals were randomly placed into one of two equally sized groups, or split-samples, in order to confirm reproducibility of the principal components identified. For the first split-sample, a matrix of correlations among frequency of consumption for the questionnaire food items was constructed and entered in the PCA. Extraction of principal components was followed by orthogonal rotation of retained components to allow for interpretability [23, 24]. The number of components to retain for rotation was based on examination of scree plots and interpretability of the components [24]; although another common strategy is to rotate all factors with eigenvalues greater than 1.0, this method has been shown to overestimate the number of components [24]. The analysis was repeated in the second split-sample to confirm reproducibility of results. Cronbach's coefficient alpha [25] was used to evaluate internal consistency for each component retained. In psychometric research, a coefficient alpha of $\geq$0.70 generally indicates acceptable reliability [26].

A component score was calculated for each dietary pattern for each individual to represent the individual's level of intake for the pattern. The score for each pattern was computed as a linear composite of the foods with meaningful loadings ($\geq$|0.20|) for only that pattern. Scores were calculated by taking the unweighted sum of standardized frequencies of intake for each food associated with the pattern. For 395 individuals who were missing responses on individual foods in any given pattern of food intake identified by principal components analysis, we imputed a value for the missing food by taking the average standardized frequency of all other non-missing foods in that pattern.

We examined construct validity of the patterns [27] by describing their associations with sociodemographic and lifestyle variables including age, level of education, place of residence (e.g., rural or urban), various health-related behaviors, and intake of selected nutrients energy-adjusted using the residual method [28].

Statistical analyses

We used linear regression models to examine associations between dietary patterns and percent breast density, and generalized estimating equations to account for autocorrelation resulting from including women from the same family [29, 30]. All models were, at a minimum, adjusted for age as a continuous variable. Final multivariate models included 1,286 women (from 311 different families) who had complete covariate data. Models adjusted for age, caloric intake, menopausal status, education (< high school, high school graduate, some college, college graduate+), physical activity (low, moderate, high), years of hormone replacement use (0, 1–5, 6+), body mass index (BMI), waist–hip ratio (WHR), age at menarche, a variable combining parity and age at first live birth (nulliparous, 1–2 children with age at first live birth >20, 1–2 children with age at first live birth $\leq$20, 3+ children with age at first live birth >20, 3+ children with age at first live birth $\leq$20), alcohol intake (servings per week), and relation to proband (first-degree relative, second-degree relative, married-in). Categorical covariates were coded using dummy variables to allow for non-linear associations across categories. Other variables evaluated as confounders but not included in final models were smoking status, years of use of oral contraceptives, history of hysterectomy, and history of oophorectomy. Because the distribution of percent density was slightly skewed, we modeled a (normally distributed) square-root transformation of percent density in additional analyses and found no meaningful differences with respect to statistically significant associations or interactions. We present results on the non-transformed variable for reasons of interpretability.

We examined the possibility of effect modification by menopausal status by examining *p*-values for interaction, estimated from a model including a variable *x* menopausal status interaction term. We used the same strategy to assess possible effect modification by relation to proband (first-degree relative, second-degree relative, married-in), overweight status (BMI $<$ 25 kg/m^2 vs. $\geq$ 25 kg/m^2), and smoking status (current vs. non-smoker).

Results

Among 3,147 women with adequate dietary information, mean (SD) age was 57 (15) years, mean (SD) BMI was 26.5 (5.6) kg/m^2, and 16% had at least a college degree (Table 1).

In PCA, three dietary patterns emerged consistently across the split samples (Table 2): (1) a "fruit–vegetable–cereal" pattern; (2) a "salad–sauce–pasta/grain" pattern with high loadings for pasta, rice, and such salad and sauce vegetables as mushrooms, garlic, peppers, lettuce, onions, and tomatoes; and (3) a "meat-starch" pattern with high loadings for French fries, fried chicken and fish, meat, white bread, cheese, eggs, and sweets.

To place these dietary patterns in context, we described the distributions of selected sociodemographic and health-related characteristics across pattern quintiles (Table 3). Women with high intake of the fruit–vegetable–cereal

Table 1 Descriptive characteristics of sample and age-adjusted betas for associations with percent breast density

Characteristic	All subjects[a] (N = 3,147)	Subjects in final model (N = 1,286)
Mean (±SD) age (y)	56.7 (±14.9)	57.0 (±11.8)
Level of education (%)		
<High school	15.1	11.2
High school graduate	36.7	38.7
Some college	31.9	32.4
College graduate +	16.3	17.8
Mean (±SD) BMI (kg/m^2)	26.5 (±5.6)	27.0 (±5.7)
Postmenopausal (%)	69	72
Smoking status (%)		
Never	55	55
Former	29	31
Current	16	14
Relation to proband		
Married in	42	37
Second-degree relative	42	46
First-degree relative	16	18
Mean dietary pattern score[b]		
Fruit-vegetable-cereal	0	0.1
Salad-sauce-pasta/grain/grain	0	0.3
Meat-starch	0	0

[a] Due to missing values, N = 2,961 for BMI, and N = 3,106 for menopausal status

[b] Mean dietary pattern scores were 0 over all subjects (N = 3,147) because frequencies of intake for all foods were standardized prior to calculating scores (see Methods section)

pattern and those with high intake of the salad–sauce–pasta/grain pattern were similar in being better-educated and more likely to exercise and to use multivitamins than women with low intake of those patterns. Unlike the fruit–vegetable–cereal pattern, however, high salad–sauce–pasta/grain pattern consumption was inversely rather than positively associated with age, was more strongly associated with a college education, was associated with living in a large city or a suburb of a large city, was associated with former rather than never smoking, and was positively rather than inversely associated with alcohol intake. Compared with women with low intake of the meat–starch pattern, those with high intake were younger, less well-educated, more likely to live in a rural area and to smoke, and less likely to use multivitamins or to exercise.

Among 1,286 women with complete covariate data, mean (SD) percent breast density was 22.6 (15.9). None of the three dietary patterns was associated with percent breast density in these women (Table 4). We saw some evidence of effect modification by menopausal status for the fruit–vegetable–cereal pattern, which was inversely, albeit nonsignificantly, associated with percent density among premenopausal women only (β = -0.13, p = 0.09; p for interaction = 0.009). Because of previous analyses that identified smoking status as an effect modifier, we examined this possibility in our data as well. We observed inverse associations with percent density for the fruit–vegetable–cereal (β = -0.30, p = 0.02; interaction p = 0.05) and salad–sauce–pasta/grain (β = −0.27, p = 0.06; interaction p = 0.006) patterns among current smokers only. We saw no clear effect modification by family history or overweight status.

Discussion

Our study is among the first to examine dietary patterns in relation to breast density. In our sample, a fruit–vegetable–cereal pattern was weakly inversely associated with percent breast density among premenopausal women. The fruit–vegetable–cereal and salad–sauce–pasta/grain patterns were inversely associated with breast density only among current smokers. We observed no association with breast density for the meat–starch dietary pattern.

Our fruit–vegetable–cereal and meat–starch patterns resemble patterns often called the "prudent" and "western" patterns in previous studies in the US [2, 4] and in Europe [1, 3]. We also identified a dietary pattern characterized by intake of pasta and other grains, salad vegetables, sauces, and legumes. That pattern, while nutritionally similar to the fruit–vegetable–cereal pattern and similar with respect to its association with physical activity and supplement use, differed from the fruit–vegetable–cereal pattern in notable ways. Compared with women with high intake of the fruit–vegetable–cereal pattern, those with high intake of the salad–pasta/grain pattern were younger, better educated, more likely to live in a large city or suburb, had lower BMI and WHR, and were more likely to be former or current rather than never smokers. Our empirical findings suggest the emergence of a new type of "prudent" pattern among younger women but require confirmation in other samples and settings.

A previous analysis of food and nutrient intake and breast density in the same sample of participants from the Minnesota Breast Cancer Family Cohort [31] showed associations of percent breast density with alcohol, polyunsaturated fat, and vitamins C and E and inverse associations for saturated fat and dairy intake among premenopausal women, while among postmenopausal women percent density was associated with intake of vitamin B_{12} and white wine and inversely associated with red wine intake. However, this previous analysis used a subjective estimate of percent density determined by an experienced radiologist. Among food-based analyses conducted in other

Table 2 Factor loadings for foods associated with each dietary pattern, in split samples of 3,147 participants in the Minnesota Breast Cancer Family Study. Factor loadings for foods associated with each dietary pattern, in split samples of 3,147 participants in the Mayo cohort

Fruit–vegetable–cereal			Salad–sauce–pasta/grain/grain			Meat–starch		
	Sample 1[a]	Sample 2[b]		Sample 1	Sample 2		Sample 1	Sample 2
Carrots, cooked	57	44	Mushrooms	55	56	French fried potatoes	47	43
String beans	53	38	Garlic	52	55	Chicken or turkey, breaded or fried	41	26
Beets	49	37	Green or chili peppers	52	45	Beef, pork, or lamb as a sandwich or hot dish	41	39
Peas or lima beans	47	29	Mustard	39	34	White bread	40	36
Yellow (winter) squash	47	40	Red chili sauce	37	36	Hot dogs	39	30
Cabbage or coleslaw	46	41	Pasta	37	40	Processed meats	39	38
Peaches, nectarines, apricots, or plums	45	40	Brown rice	33	30	Cheese	37	34
Bananas	43	36	Alfalfa sprouts	33	36	Eggs	36	38
Applesauce	42	42	Shrimp, lobster, scallops	27	34	Fish, fried, battered, or breaded	35	32
Yams or sweet potatoes	42	45	English muffins, bagels, rolls, or buns	26	20	Beef, pork, or lamb as a main dish	34	39
Pineapple	38	37	White rice	25	26	Pizza	34	36
Oranges	38	40	Grains (e.g., bulgar, kasha, couscous)	24	22	Bacon	33	42
Celery	38	37	Onions, raw	48	45	Doughnuts	32	30
Pears	36	40	Romaine or leaf lettuce	47	51	Candy bars	32	29
Vegetable or noodle soup	35	30	Onions, cooked	44	43	Hamburger, lean	31	35
Other fruits, fresh, frozen or canned, e.g., fruit cocktail	35	32	Tomato sauce	40	42	Butter	31	34
Apples	34	48	Spinach, cooked	38	38	Regular mayonnaise or creamy salad dressing	31	44
Bean, pea, or lentil soup	34	35	Tomatoes	37	34	Hamburger, regular	31	50
Cantaloupe	33	34	Iceberg or head lettuce	36	35	Potato or corn chips	30	35
Strawberries	33	32	Beans, lentils, chili beans, or garbanzos, baked or dried	35	35	Brownies	30	32
Carrots, raw	33	37	Lowfat mayonnaise	25	28	Salt	29	35
Grapefruit	32	34				Chicken or turkey with skin	28	33
Oatmeal	31	40				Pancakes or waffles	28	21
Other cooked breakfast cereal	30	26				Ice cream	28	27
Blueberries	27	25				Chowder or cream soup	27	24
Grapes	27	26				Sweet roll, coffee cake, or other pastry, ready made	25	33
Watermelon	27	29				Coffee	22	22
Lowfat cottage or ricotta cheese	26	28				Chocolate	20	24
Dried apricots, peaches, or nectarines	26	31						
Bran or oat muffins or biscuits	25	21						
Raisins	24	26						

Table 2 continued

Fruit–vegetable–cereal			Salad–sauce–pasta/grain/grain		Meat–starch	
	Sample 1[a]	Sample 2[b]	Sample 1	Sample 2	Sample 1	Sample 2
Whole wheat or whole grain bread	23	22				
Orange juice	21	22				
Honeydew	21	23				
% Variance	8.0	6.8	5.3	6.0	4.8	5.1
Coefficient alpha	0.82	0.82	0.76	0.77	0.73	0.74

[a] $N = 1{,}579$

[b] $N = 1{,}568$

Table 3 Sociodemographic and health behavior characteristics for first and fifth dietary pattern quintiles in 3,147 participants[a] in the Minnesota Breast Cancer Family Study

	Fruit–vegetable–cereal quintiles		Salad–sauce–pasta/grain quintiles		Meat–starch quintiles	
	1	5	1	5	1	5
Mean (SD) age (y)	48.7 (14.3)	63.6 (13.6)[b]	60.4 (15.4)	54.5 (14.1)[b]	60.5 (13.8)	53.2 (14.9)[b]
Level of education (%)						
<High school	15	17	22	9	13	15
High school graduate	44	31	46	28	35	43
Some college	29	33	25	36	36	30
College graduate+	12	19[c]	8	28[b]	17	11[c]
Place of residence (%)						
Large city or suburb	43	38	30	51	48	32
Rural area	20	20	27	15	14	25
Other	37	42	42	34[b]	38	43[b]
Mean (±SD) BMI (kg/m^2)	25.9 (5.6)	27.1 (5.9)[c]	26.4 (5.4)	26.3 (5.6)	25.7 (4.8)	27.7 (7.0)[b]
Mean (±SD) WHR	0.8 (0.1)	0.9 (0.1)[b]	0.9 (0.1)	0.8 (0.1)[b]	0.8 (0.1)	0.8 (0.1)
Level of physical activity (%)						
Low	45	22	45	23	24	36
Moderate	29	33	32	31	32	35
High	26	45[b]	22	46[b]	44	29[b]
Smoking status (%)						
Never smoked	43	68	59	51	57	49
Former smoker	27	26	24	35	35	25
Current smoker	31	6[b]	17	14[c]	9	26[b]
Supplement use (%)	58	74[b]	61	73[b]	76	60[b]
Pearson correlations[d]						
Energy (kcal)	0.51[b]		0.43[b]		0.66[b]	
Total fat	−0.41[b]		−0.28[b]		0.55[b]	
Saturated fat	−0.44[b]		−0.31[b]		0.55[b]	
Fiber	0.65[b]		0.42[b]		−0.39[b]	
Carotenoids	0.49[b]		0.26[b]		−0.25[b]	
Folate	0.45[b]		0.40[b]		−0.36[b]	

[a] Due to missing values, $N = 2{,}961$ for BMI, $N = 3{,}026$ for WHR, $N = 3{,}144$ for urban/rural

[b] $P < 0.0001$; P-values were determined by Cochran-Mantel-Haenszel test statistic for categorical variables or by analysis-of-variance of continuous variables

[c] $P < 0.01$

[d] Correlations with energy-adjusted nutrients

Table 4 Multivariate-adjusted[a] betas for association with percent breast density and mean percent densities for quintiles 1 and 5 for each dietary pattern ($N = 1{,}286$)

	Beta[b] (SE)	*p*-value	Quintile[c] 1	Quintile 5
Fruit–vegetable–cereal	0.01 (0.03)	0.7	24.5	23.9
Premenopausal[d]	−0.13 (0.08)	0.09	31.2	28.3
Postmenopausal	0.03 (0.03)	0.37	19.4	19.2
Interaction *P*		0.009		
Current smoker[d]	−0.30 (0.13)	0.02	31.4	25.0
Nonsmoker	0.03 (0.04)	0.48	23.4	23.7
Interaction *P*		0.05		
Salad–sauce–pasta/grain	0.01 (0.04)	0.8	23.3	24.4
Premenopausal	−0.10 (0.09)	0.26	30.3	28.2
Postmenopausal	0.04 (0.05)	0.48	18.2	19.9
Interaction *P*		0.06		
Current smoker	−0.27 (0.15)	0.06	26.4	22.4
Nonsmoker	0.03 (0.05)	0.48	23.4	24.4
Interaction *P*		0.006		
Meat–starch	0.04 (0.04)	0.3	23.4	25.5
Premenopausal	0.07 (0.08)	0.40	30.0	33.2
Postmenopausal	0.03 (0.05)	0.55	19.5	20.4
Interaction *P*		0.12		
Current smoker	0.14 (0.11)	0.18	24.0	28.4
Nonsmoker	0.04 (0.04)	0.40	23.9	25.8
Interaction *P*		0.62		

[a] Adjusted for age, caloric intake, menopausal status, education, physical activity, years of use of hormone replacement, BMI, WHR, age at menarche, parity and age at first live birth (combined variable), alcohol intake, and relation to proband

[b] Betas represent absolute mean change in percent breast density per unit increment in dietary pattern score

[c] Quintiles were defined for $N = 1{,}286$ women in unstratified analyses, and separately for each stratum in stratified analysis

[d] $N = 356$ premenopausal, 930 postmenopausal

[e] $N = 176$ current smokers, 1,110 nonsmokers

populations, one study reported a positive association between meat intake and breast density [32]. Another [33] reported an inverse association between vegetable intake and breast density, but two others did not [32, 34]. In nutrient-based analyses, several studies reported positive associations for total and saturated fat, protein, and alcohol intake [32, 33, 35–38], and inverse associations for intake of fiber, carotenoids, calcium, and vitamin D [33, 35, 39–42]. The generally inconsistent evidence for an association between diet and mammographic density in previous studies leaves open the possibility that mammographic density may not mediate dietary effects, if any, on breast cancer.

The only previous study to have examined dietary patterns in relation to breast density found a suggestive association with breast density for a "fat and meat" and an inverse association for a "vegetables" pattern, but neither was statistically significant [15]. It is also informative to compare the current findings with previous studies that have examined dietary patterns and risk of breast cancer. With the exception of a case–control study conducted in Uruguay [7], they have generally found little evidence for an association of either a "prudent" or "western" pattern with breast cancer risk [1–5]. In the Nurses' Health Study, the prudent pattern was inversely associated only with ER- postmenopausal breast cancer [2]. In the Swedish Mammography Screening Cohort, breast cancer risk was moderately increased only for women in the highest category of the "drinker" dietary pattern, characterized chiefly by intake of wine, liquor, and beer [1]. In other studies, breast cancer risk was inversely related to intake of a "salad vegetables" pattern in Italy, characterized by intake of raw vegetables and olive oil [3], a "pork, processed meat, potatoes" pattern in the Netherlands cohort [6], and a traditional southern pattern in the US [4].

We observed inverse associations for the fruit–vegetable–cereal and salad–sauce–pasta/grain dietary patterns only among smokers. Our observation is consistent with the finding of an inverse association of the prudent pattern with premenopausal breast cancer only among smokers in the Nurses' Health Study [5]. Similarly, in the Breast Cancer Detection Demonstration Project, the protective effect of the traditional southern pattern for postmenopausal breast cancer was apparent only among smokers [4]. Previous investigators have hypothesized that diets high in antioxidants have a visibly protective effect against cancer-promoting properties of smoking. If this is so, then our findings would suggest the protective potential for diet modification among smokers, with early, visible effects on breast density. In our sample, however, smoking itself was not associated with increased breast density, and the applicability of this hypothesis to our findings is unclear.

Measurement error in dietary assessment may have limited our ability to detect and quantify dietary patterns, but replication across split samples and high coefficient values for Cronbach's alpha indicate good reproducibility and internal reliability for all three patterns. In addition, nonparticipation in the mammography phase of the study may have biased estimates of the association between dietary intake and breast density. A previous analysis [31] indicated that women at higher risk for dense breasts and women with a more health-conscious lifestyle were more likely to participate in the study. This is supported in the present analysis by our finding (Table 1) that women included in the dietary pattern–breast density analyses ($N = 1{,}286$) had higher mean scores for the fruit–vegetable–cereal and

salad–sauce–pasta/grain dietary patterns than women in the dietary pattern analyses ($N = 3{,}147$). Overrepresentation of such women in our sample likely biased our estimates for those particular patterns toward the null.

A strength of the study is its relatively large sample size for both dietary pattern analyses and analyses relating dietary pattern intake to breast density estimates. An additional strength is its use of quantitative estimates of breast density that were also highly reliable. Our analyses were based on mediolateral mammographic views whereas most previous studies used cranial–caudal views. But correlations for percent density between mediolateral and cranial–caudal view estimates for the 1,169 women in our sample with both views were high ($r > 0.85$), and additional analyses using cranial–caudal views in the smaller sample of women with those images ($N = 1{,}041$) showed similar results.

Overall our results do not provide strong evidence for overall associations of dietary patterns with breast density, consistent with most previous studies on dietary patterns and breast cancer risk. Suggestive inverse associations for fruit–vegetable–cereal and salad–sauce–pasta/grain dietary patterns among smokers are also consistent with other reports in the literature, and they leave open the possibility that some dietary patterns might influence breast density in certain subsets of the population. Nevertheless, these findings require confirmation, and the reasons underlying these observations have yet to be clarified.

Acknowledgments The authors thank Ms. Xiaoxing He for her assistance in data analysis, and Ms. Fang-Fang Wu for her work in reading mammograms. Grant support: Supported by grant 5 R03 CA097779-02 from the National Institutes of Health.

References

1. Terry P et al (2001) A prospective study of major dietary patterns and the risk of breast cancer. Cancer Epidemiol Biomarkers Prev 10:1281–1285
2. Fung TT et al (2005) Dietary patterns and the risk of postmenopausal breast cancer. Int J Cancer 116(1):116–121
3. Sieri S et al (2004) Dietary patterns and risk of breast cancer in the ORDET cohort. Cancer Epidemiol Biomarkers Prev 13:567–572
4. Velie EM et al (2005) Empirically derived dietary patterns and risk of postmenopausal breast cancer in a large prospective cohort study. Am J Clin Nutr 82(6):1308–1319
5. Adebamowo CA et al (2005) Dietary patterns and the risk of breast cancer. Ann Epidemiol 15(10):789–795
6. Mannisto S et al (2005) Dietary patterns and breast cancer risk: results from three cohort studies in the DIETSCAN project. Cancer Causes Control 16(6):725–733
7. Ronco AL et al (2006) Food patterns and risk of breast cancer: a factor analysis study in Uruguay. Int J Cancer 119(7):1672–1678
8. Byrne C (1997) Studying mammographic density: implications for understanding breast cancer. J Natl Cancer Instit 89:531–533
9. Maskarinec G, Meng L (2000) A case–control study of mammographic densities in Hawaii. Breast Ca Res Treatment 63:153–161
10. Ursin G et al (2003) Mammographic density and breast cancer in three ethnic groups. Cancer Epidemiol Biomarkers Prev 12:332–338
11. Brisson J et al (2000) Tamoxifen and mammographic breast densities. Cancer Epidemiol Biomarkers Prev 9:911–915
12. Greendale GA et al (2003) Postmenopausal hormone therapy and change in mammographic density. J Natl Cancer Instit 95:30–37
13. Freedman M et al (2001) Digitized mammography: a clinical trial of postmenopausal women randomly assigned to receive raloxifene, estrogen, or placebo. J Natl Cancer Instit 93:51–56
14. Kerlikowske K et al (2007) Longitudinal measurement of clinical mammographic breast density to improve estimation of breast cancer risk. J Natl Cancer Inst 99(5):386–395
15. Takata Y et al (2007) Mammographic density and dietary patterns: the multiethnic cohort. Eur J Cancer Prev 16(5):409–414
16. Sellers TA et al (1995) Epidemiologic and genetic follow-up study of 544 Minnesota breast cancer families: design and methods. Genet Epidemiol 12:417–429
17. Sellers TA et al (1999) Fifty-year follow-up of cancer incidence in a historical cohort of Minnesota breast cancer families. Cancer Epidemiol Biomarkers Prev 8(12):1051–1057
18. Weaver TW et al (1996) Validation study of self-reported measures of fat distribution. Int J Obes Relat Metab Disord 20(7):644–650
19. Willett WC et al (1988) The use of a self-administered questionnaire to assess diet four years in the past. Am J Epidemiol 127:188–199
20. Byng JW, Boyd NF, Fishell E (1994) The quantitative analysis of mammographic densities. Phys Med Biol 39:1629–1638
21. McCormack VA, dos Santos Silva I (2006) Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev 15(6):1159–1169
22. Vachon CM et al (2007) Mammographic breast density as a general marker of breast cancer risk. Cancer Epidemiol Biomarkers Prev 16(1):43–49
23. Kleinbaum DG, Kupper LL, Muller KE (1988) *Applied regression analysis and other multivariable methods* 2nd edn. Duxbury Press, Belmont, CA
24. Kline P (1994) An easy guide to factor analysis. Routledge, New York
25. Cronbach LJ (1951) Coefficient alpha and the internal structure of tests. Psychometrika 16:297–334
26. Nunnally J (1978) Psychometric theory. McGraw-Hill, New York
27. DeVellis RF (1991) Scale development theory and applications. Applied social research methods series Vol. 26. SAGE Publications, Newbury Park, CA
28. Willett W, Stampfer M (1986) Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 124:17–27
29. Williamson JM, Lipsitz SR, Kim KM (1999) GEECAT and GEEGOR: computer programs for the analysis of correlated categorical response data. Comput Methods Programs Biomed 58:25–34
30. Zeger SL, Liang KY (1986) Longitudinal data analysis for discrete and continuous outcomes. Biometrics 42:121–130
31. Vachon CM et al (2000) Association of diet and mammographic breast density in the Minnesota breast cancer family cohort. Cancer Epidemiol Biomarkers Prev 9:151–160
32. Sala E et al (2000) High risk mammographic parenchymal patterns and diet: a case–control study. British J Cancer 83:121–126
33. Masala G et al (2006) Dietary and lifestyle determinants of mammographic breast density. A longitudinal study in a Mediterranean population. Int J Cancer 118(7):1782–1789
34. Jakes RW et al (2002) Mammographic parenchymal patterns and self-reported soy intake in Singapore Chinese women. Cancer Epidemiol Biomarkers Prev 11:608–613

35. Brisson J et al (1989) Diet, mammographic features of breast tissue, and breast cancer risk. Am J Epidemiol 130:14–24
36. Boyd NF et al (1997) Effects at two years of a low-fat, high-carbohydrate diet on radiologic features of the breast: results from a randomized trial. J Natl Cancer Inst 89:488–496
37. Nagata C et al (2005) Associations of mammographic density with dietary factors in Japanese women. Cancer Epidemiol Biomarkers Prev 14:2877–2880
38. Boyd NF et al (1995) Plasma lipids, lipoproteins, and mammographic densities. Cancer Epidemiol Biomarkers Prev 4: 727–733
39. Nagel G et al (2005) Dietary phytoestrogen intake and mammographic density—results of a pilot study. Eur J Med Res 10(9):389–394
40. Bérubé S et al (2005) Vitamin D and calcium intakes from food or supplements and mammographic breast density. Cancer Epidemiol Biomarkers Prev 14:1653–1659
41. Bérubé S et al (2004) Vitamin D, calcium, and mammographic breast densities. Cancer Epidemiol Biomarkers Prev 13:1466–1472
42. Nordevang E et al (1993) Dietary habits and mammographic patterns in patients with breast cancer. Breast Ca Res Treatment 26:207–215