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Article

Diet Quality and Breast Cancer Recurrence and Survival: The Pathways Study

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Abstract

Background: Prior research suggests a relationship between overall diet quality and breast cancer survival, although few studies have reported on this topic. We evaluated whether 4 dietary quality indices consistent with healthy eating recommendations around the time of breast cancer diagnosis were associated with risk of recurrence, cause-specific, and all-cause mortality. **Methods:** A total of 3660 women diagnosed with invasive breast cancer were included. Diet was assessed an average of 2.3 (range = 0.7-18.7) months after diagnosis, from which 4 dietary quality indices were derived: the American Cancer Society guidelines (ACS), the alternate Mediterranean Diet Index (aMED), the Dietary Approaches to Stop Hypertension (DASH), and the 2015 Healthy Eating Index (HEI). Over 40 888 person-years of follow-up, 461 breast cancer recurrences, and 655 deaths were ascertained. Cox models were used to estimate hazards ratios (HRs) and 95% confidence intervals (CIs). **Results:** Adjusted comparisons between extreme quintiles showed all 4 dietary quality indices to be inversely associated with all-cause mortality, suggesting a 21%-27% lower risk (ACS HR = 0.73, 95% CI = 0.56 to 0.95; aMED HR = 0.79, 95% CI = 0.61 to 1.03; DASH HR = 0.76, 95% CI = 0.58 to 1.00; HEI HR = 0.77, 95% CI = 0.60 to 1.01). Similar patterns were noted for non-breast cancer mortality (ACS HR = 0.69, 95% CI = 0.48 to 0.98; aMED HR = 0.73, 95% CI = 0.50 to 1.05; DASH HR = 0.55, 95% CI = 0.38 to 0.79; HEI HR = 0.67, 95% CI = 0.48 to 0.94). None of the dietary quality indices were associated with recurrence or breast cancer–specific mortality. **Conclusion:** Food intake patterns concordant with dietary quality indices consistent with recommendations for healthy eating may be beneficial for women with breast cancer.

It is estimated that there are more than 3.5 million breast cancer survivors living in the United States (1). After a breast cancer diagnosis, women are highly motivated to make lifestyle changes and have expressed a desire for more evidence-based information from health professionals (2,3). A growing body of research has evaluated diet and breast cancer survival, focusing mostly on individual foods and nutrients (4-7). While providing insight into biological mechanisms, national dietary guidelines are typically presented as dietary patterns, not individual foods (8).

A dietary pattern index is the composite measure of the quantities and portions of all foods, drinks, and nutrients in one's diet as well as the frequency with which they are consumed (9). Studies have used both data driven and a priori dietary quality indices to examine concordance with healthy dietary patterns and breast cancer survival (10-14). However, methodological issues concerning timing of dietary assessment relative to diagnosis, inconsistent exposure assessment, and absence of secondary outcomes have made comparability challenging.

To our knowledge, only 1 other study has assessed multiple a priori dietary quality indices among a cohort of breast cancer survivors enrolled near the time of their diagnosis (15). The Shanghai Breast Cancer Survival Study (SBCSS) reported that comparisons of extreme quartiles from both the Chinese Food

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Pagoda and Dietary Approaches to Stop Hypertension (DASH) dietary indices were associated with a lower risk of total mortality and breast cancer–specific events (15).

Our study examined 4 a priori dietary quality indices estimated from dietary data collected soon after breast cancer diagnosis, with breast cancer recurrence and cause-specific and all-cause mortality, among a cohort of breast cancer survivors in the United States. The dietary quality indices of interest were an index based on the American Cancer Society nutrition guidelines (ACS) (16), the alternate Mediterranean Diet Index (aMED) (17), an index based on the DASH diet (18), and the 2015 Healthy Eating Index (HEI) (19).

Methods

Study Cohort

The Pathways Study is a prospective cohort of 4505 female breast cancer survivors diagnosed with breast cancer between the years 2005 and 2013 from Kaiser Permanente Northern California (KPNC); further details on this study are provided elsewhere (20). Briefly, diet was assessed an average of 2.3 (range = 0.7-18.7) months after diagnosis. Eligibility criteria included being female; aged 21 years or older; KPNC membership; speaking English, Spanish, Cantonese, or Mandarin; living within a 65-mile radius of a field interviewer; diagnosis of incident invasive breast cancer; and no prior history of other invasive cancers. The enrollment rate was 40.3% of those eligible (4505 of 11 174), and participants received an in-person baseline interview administered by field staff.

This study was approved by the institutional review boards of KPNC and University of California, Berkeley. Written informed consent was obtained from all study participants.

Dietary Assessment

Dietary intake was assessed at baseline with a modified version of the Block 2005 Food Frequency Questionnaire (21). Its 139 food items and additional questions were selected to be representative of a wide range of dietary factors, as well as to capture foods that are popular in Hispanic and Asian populations.

Among the 4505 women in the cohort, 782 (17.4%) were excluded from this analysis because they did not complete the dietary assessment at baseline. An additional 63 (1.4%) participants were excluded because of estimated daily total energy intake (kcal/d) being less than 400 or greater than 4000. Although no statistically significant differences were observed in regard to survival outcomes, excluded participants were less likely to be older, White, educated, postmenopausal, nonsmokers, and estrogen receptor (ER) positive as compared with those included in the analysis (Supplementary Table 1, available online). These exclusions brought the final sample size to 3660.

Dietary Quality Indices

Four a priori dietary quality indices were created to assess concordance with dietary patterns at baseline: ACS, aMED, DASH, and HEI (Supplementary Table 2, available online). Whereas ACS was selected because of its direct relevance to cancer-specific outcomes, the others were chosen because of their prior demonstrated associations with cancer prevention (22-24) and survival (11,12,25). For all 4 dietary quality indices, a higher score is indicative of a food and nutrient intake that is more concordant with a healthful dietary pattern.

ACS Score

The ACS score ranges from 0 to 9 and has 3 main components: total fruits and vegetables (which rewards variety for those consuming at least 5 different fruits or vegetables per month), whole grains as a percentage of total grains, and total red and processed meats. Each component is worth 0 (lowest) to 3 (highest) points and is based on cohort-specific quartiles for that component (red and processed meat score is reversed) (16).

aMED Score

The aMED score is comprised of 9 dietary components, 7 to be encouraged and 2 to be moderated. The encouraged components include vegetables, legumes, fruits, nuts, whole grains, seafood, and the ratio of monosaturated to saturated fats, and the moderated components are alcohol and red and processed meats. Intakes above the population median for encouraged components received 1 point, and all other intakes received 0 points. The red and processed meat component is reverse scored, and those consuming alcohol between 5 and 15 grams per day received 1 point, and all others 0 points. Scores for this index range between 0 and 9 points (26).

DASH Score

The DASH score was calculated by creating 8 dietary components worth 5 points each from population quintiles ranging from 1 (lowest) to 5 (highest). Total scores range from 0 to 40 by combining scores from the favorable components (fruits, vegetables, nuts, grains, and low-fat dairy) and reverse scored adverse components (sodium, red and processed meats, and sugar-sweetened beverages) (18).

2015 HEI Score

The HEI, designed to align with the 2010-2015 Dietary Guidelines for Americans, is scored from a total of 13 dietary subcomponents (19). Six of these (total fruits, whole fruits, total vegetables, greens and beans, total protein foods, and seafood and plant protein foods) are worth 5 points each, and 7 others (whole grains, dairy, fatty acids, refined grains, sodium, added sugars, and saturated fats) are worth 10 points each, for a total possible score of 100 points. The HEI is the only index in this analysis for which every component is scored on a density basis (per 1000 kcal or percentage of energy), except for fatty acids, which is the ratio of unsaturated to saturated fats (19).

Covariates

Demographic and behavioral factors including age, race and ethnicity, education, menopausal status, smoking status, physical activity, and body mass index (BMI) were collected using the baseline questionnaire at time of entry. Where possible, missing data were supplemented with data obtained from the KPNC electronic health records and medical chart review (MCR), except in the case of BMI, where the electronic health records data took precedence over self-reported values. Diagnostic and clinical data, which included tumor stage; ER, progesterone receptor (PR), and HER2 status; type of surgery; and receipt of chemotherapy, radiation, and hormonal therapies, were ascertained from a combination of the KPNC Cancer Registry and other clinical databases.

Outcomes Ascertainment

The primary outcomes for this study include breast cancer recurrence, breast cancer–specific mortality, nonbreast cancer–specific mortality, and all-cause mortality. Recurrences were ascertained either during follow-up interviews with participants or from monthly algorithmic searches of KPNC electronic databases. All recurrences were confirmed by MCR. Deaths and causes of death were identified during follow-up interviews with relatives of participants and then confirmed by MCR or from linkages with data from the state of California, the Social Security Administration, and the National Death Index. Over the course of 40,888 person-years, there were 461 (12.6%) recurrences, 324 (8.9%) deaths due to breast cancer, 331 (9.0%) deaths due to causes other than breast cancer, and 655 (17.9%) deaths due to any cause.

Statistical Analysis

Spearman correlation coefficients were used to compare the total scores of the dietary quality indices, and cohort-specific quintiles of each dietary quality index were calculated. Cox models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) to assess the association between each dietary quality index and recurrence and breast cancer–specific, nonbreast cancer–specific, and all-cause mortality. In all models, the lowest scoring group was used as the reference group for each index. Models with dietary quality indices expressed as linear splines were considered (27), but a simple linear term was favored in formal comparisons based on the Bayes information criterion. Trend results corresponding to a 1-unit increase in each index using the noncategorized variable are presented.

Because women entered the cohort after their initial breast cancer diagnosis, they were not considered at risk for a possible outcome before their baseline dietary assessment. Therefore, delayed-entry models were used, and person-time was calculated from the date of completion of the baseline questionnaire to the date of first confirmed breast cancer recurrence or date of death, depending on the analysis. Those participants without an event were censored at the end of the study period: December 31, 2018.

Three separate models for each index were evaluated: the first (model 1) was adjusted for age at diagnosis and total energy intake. Because Food Frequency Questionnaires are known to result in greater variance in estimates of food and nutrient intake than may be biologically plausible, we adjust for total energy in all models to diminish the impact of this extraneous variance (28). The second model (model 2) was adjusted for the variables in model 1 and race and ethnicity; education level; menopausal status; physical activity; smoking; cancer stage at diagnosis; and ER, PR, and HER2. These are variables that, to our knowledge, unambiguously satisfy the criteria for confounding the relationship between diet and survival (Supplementary Figure 1, available online). The third model (model 3) included all variables in model 2 and BMI, type of surgery, chemotherapy, radiation, and hormonal therapies. These additional variables were identified as factors that may lie on the causal pathway between diet at breast cancer diagnosis and survival (Supplementary Figure 1, available online).

Subanalyses were conducted to examine the independent associations between the individual food components from each index and all-cause mortality. Separate models were estimated for each food component while adjusting for all variables in model 2 and the other components in the index being evaluated. Adjusted models containing interaction terms for each dietary quality index score and each of chemotherapy, radiation, ER, PR, and HER2 were also assessed.

All statistical analyses were conducted using SAS 9.4 software (SAS Institute, Cary, NC). Figures were generated using R software (29).

Results

Baseline Characteristics

The mean age of participants at diagnosis was 59.7 (range = 24-94) years, and women in the highest category of the ACS score as compared with the lowest were more likely to be older, White, more educated and physically active, postmenopausal, and nonsmokers and have lower BMI and lower reported energy intake at baseline. They were also more likely to be PR negative and to have received radiation therapy and less likely to have received chemotherapy (Table 1). Differences in participant characteristics across categories of the other dietary quality indices were qualitatively similar to those seen for ACS, except in the case of aMED and DASH, where respondents in the highest category reported higher energy intake as compared with those in the lowest.

Dietary Quality Indices and Study Outcomes

All 4 dietary quality indices were inversely associated with all-cause mortality when adjusting for age at diagnosis and total energy intake (Table 2). Tests for linear trend were statistically significant for ACS and HEI. Although the results in model 2 were somewhat attenuated when compared with model 1, they were relatively consistent. The direction and magnitude of each dietary quality index in model 2 were associated with a lower risk of all-cause mortality when comparing high and low score categories (ACS HR = 0.73, 95% CI = 0.56 to 0.95; aMED HR = 0.79, 95% CI = 0.61 to 1.03; DASH HR = 0.76, 95% CI = 0.58 to 1.00; HEI HR = 0.77, 95% CI = 0.60 to 1.01). Additionally, accounting for BMI and treatment variables in model 3 did not notably change the results.

All 4 dietary quality indices were inversely associated with nonbreast cancer–specific mortality when comparing high to low categories and adjusting for the variables in model 2 (ACS HR = 0.69, 95% CI = 0.48 to 0.98; aMED HR = 0.73, 95% CI = 0.50 to 1.05; DASH HR = 0.55, 95% CI = 0.38 to 0.79; HEI HR = 0.67, 95% CI = 0.48 to 0.94) (Table 3). The tests for linear trend were statistically significant for all dietary quality indices except for aMED. No associations were observed between the dietary quality indices and breast cancer–specific outcomes.

Subanalyses

Table 4 presents the associations for each index-specific dietary component and all-cause mortality after adjusting for variables in model 2 and the other dietary components in each index. Greater intake of whole grains in the case of ACS (HR = 0.91,

Table 1. Baseline characteristics of the Pathways Study participants across quintiles of ACS (n = 3660)

Characteristic	Quintiles of ACS score					P
	Q1 (n = 1282)	Q2 (n = 655)	Q3 (n = 586)	Q4 (n = 503)	Q5 (n = 634)	
Continuous, mean (SD)[a]						
Age at diagnosis, y	57.6 (11.9)	58.9 (12.2)	60.6 (11.7)	61.9 (11.8)	62.0 (11.0)	<.001
Physical activity, MET h/wk[b]	45.3 (31.1)	53.9 (34.5)	55.7 (36.5)	56.4 (34.7)	67.3 (41.0)	<.001
BMI, kg/m^2	29.9 (7.3)	28.8 (7.1)	28.2 (6.4)	27.4 (5.7)	26.3 (5.2)	<.001
Energy intake, kcal/d	1531.5 (612.7)	1499.7 (616.0)	1453.5 (560.8)	1341.9 (510.6)	1410.1 (439.5)	<.001
Categorical, No. (%)[c]						
Race/ethnicity						.001
White	817 (63.7)	431 (65.8)	397 (67.7)	371 (73.8)	475 (74.9)	
Black	91 (7.1)	43 (6.6)	43 (7.3)	28 (5.6)	35 (5.5)	
Asian/Pacific Islander	182 (14.2)	93 (14.2)	77 (13.1)	60 (11.9)	63 (9.9)	
Hispanic	163 (12.7)	72 (11.0)	56 (9.6)	35 (7.0)	52 (8.2)	
American Indian/Alaska Native	29 (2.3)	16 (2.4)	13 (2.2)	9 (1.8)	9 (1.4)	
Education						<.001
High school or less	240 (18.7)	115 (17.6)	77 (13.1)	59 (11.7)	56 (8.8)	
Some college	467 (36.4)	228 (34.8)	197 (33.6)	169 (33.6)	184 (29.0)	
College graduate	375 (29.3)	178 (27.2)	155 (26.5)	145 (28.8)	171 (27.0)	
Postgraduate	199 (15.5)	133 (20.3)	157 (26.8)	130 (25.8)	223 (35.2)	
Unknown	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	
Menopausal status						<.001
Premenopausal	453 (35.3)	214 (32.7)	144 (24.6)	114 (22.7)	135 (21.3)	
Postmenopausal	829 (64.7)	441 (67.3)	442 (75.4)	389 (77.3)	499 (78.7)	
Smoking status						<.001
Never	699 (54.5)	385 (58.8)	361 (61.6)	301 (59.8)	346 (54.6)	
Former	490 (38.2)	247 (37.7)	206 (35.2)	192 (38.2)	273 (43.1)	
Current	92 (7.2)	22 (3.4)	17 (2.9)	9 (1.8)	14 (2.2)	
Unknown	1 (0.1)	1 (0.2)	2 (0.3)	1 (0.2)	1 (0.2)	
Cancer stage						.22
I	679 (53.0)	337 (51.5)	329 (56.1)	300 (59.6)	363 (57.3)	
II	447 (34.9)	243 (37.1)	197 (33.6)	155 (30.8)	208 (32.8)	
III	133 (10.4)	66 (10.1)	52 (8.9)	44 (8.7)	51 (8.0)	
IV	23 (1.8)	9 (1.4)	8 (1.4)	4 (0.8)	12 (1.9)	
ER status						.89
Positive	1079 (84.2)	548 (83.7)	491 (83.8)	428 (85.1)	526 (83.0)	
Negative	201 (15.7)	107 (16.3)	95 (16.2)	75 (14.9)	108 (17.0)	
Unknown	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
PR status						.02
Positive	837 (65.3)	433 (66.1)	370 (63.1)	335 (66.6)	372 (58.7)	
Negative	441 (34.4)	221 (33.7)	216 (36.9)	168 (33.4)	262 (41.3)	
Unknown	4 (0.3)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	
HER2 status						.36
Positive	166 (12.9)	85 (13.0)	88 (15.0)	53 (10.5)	80 (12.6)	
Negative	1063 (82.9)	547 (83.5)	484 (82.6)	429 (85.3)	522 (82.3)	
Unknown	53 (4.1)	23 (3.5)	14 (2.4)	21 (4.2)	32 (5.0)	
Surgery type						.19
Lumpectomy	755 (58.9)	364 (55.6)	361 (61.6)	321 (63.8)	379 (59.8)	
Mastectomy	484 (37.8)	265 (40.5)	207 (35.3)	166 (33.0)	239 (37.7)	
None	43 (3.4)	26 (4.0)	18 (3.1)	15 (3.0)	15 (2.4)	
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	
Chemotherapy						<.001
No	616 (48.0)	341 (52.1)	322 (54.9)	291 (57.9)	368 (58.0)	
Yes	662 (51.6)	311 (47.5)	263 (44.9)	211 (41.9)	264 (41.6)	
Unknown	4 (0.3)	3 (0.5)	1 (0.2)	1 (0.2)	2 (0.3)	
Radiation therapy						.009
No	752 (58.7)	372 (56.8)	326 (55.6)	252 (50.1)	334 (52.7)	
Yes	530 (41.3)	283 (43.2)	260 (44.4)	251 (49.9)	300 (47.3)	
Hormonal therapy						.22
No	308 (24.0)	147 (22.4)	154 (26.3)	119 (23.7)	174 (27.4)	
Yes	963 (75.1)	504 (76.9)	427 (72.9)	382 (75.9)	457 (72.1)	
Unknown	11 (0.9)	4 (0.6)	5 (0.9)	2 (0.4)	3 (0.5)	

[a]Analysis of variance. ACS = American Cancer Society nutrition guidelines score; BMI = body mass index; ER = estrogen receptor; MET = metabolic equivalent of task; PR = progesterone receptor; Q = quintile.
[b]There were 4 participants with unknown physical activity.
[c]Pearson χ^2 test.

Table 2. Hazards ratios and 95% confidence intervals of quintiles of dietary quality indices and all-cause mortality

		Model 1[a] (n = 3660)				Model 2[b] (n = 3506)				Model 3[c] (n = 3471)			
Dietary index	Range	Events	PT, y	HR (95% CI)	HR (P_{trend})	Events	PT, y	HR (95% CI)	HR (P_{trend})	Events	PT, y	HR (95% CI)	HR (P_{trend})
ACS					0.93 (<.001)				0.96 (.04)				0.96 (.07)
Q1	0-3	237	11 792.3	Referent		232	11 271.5	Referent		226	11 148.5	Referent	
Q2	4	128	5954.7	1.00 (0.81 to 1.25)		124	5746.4	1.00 (0.80 to 1.25)		122	5683.9	1.02 (0.81 to 1.27)	
Q3	5	99	5363.6	0.80 (0.64 to 1.02)		98	5211.6	0.90 (0.71 to 1.15)		95	5172.1	0.90 (0.71 to 1.16)	
Q4	6	96	4639.8	0.84 (0.66 to 1.07)		93	4425.8	1.01 (0.78 to 1.29)		92	4409.8	1.03 (0.80 to 1.33)	
Q5	7-9	95	5817.2	0.67 (0.53 to 0.85)		87	5516.2	0.73 (0.56 to 0.95)		86	5466.2	0.77 (0.59 to 1.01)	
aMED					0.91 (<.001)				0.96 (.10)				0.97 (.27)
Q1	0-2	177	7349.3	Referent		171	7011	Referent		170	6908.0	Referent	
Q2	3	116	5628.9	0.84 (0.67 to 1.07)		114	5425.2	1.07 (0.84 to 1.36)		111	5380.1	1.08 (0.85 to 1.39)	
Q3	4	119	5983.4	0.83 (0.65 to 1.05)		114	5743.0	1.02 (0.79 to 1.30)		112	5694.5	1.05 (0.82 to 1.35)	
Q4	5	117	5584.4	0.87 (0.68 to 1.11)		113	5401.7	1.13 (0.87 to 1.46)		107	5346.2	1.17 (0.90 to 1.53)	
Q5	6-9	126	9021.7	0.56 (0.43 to 0.71)		122	8590.6	0.79 (0.61 to 1.03)		121	8551.5	0.87 (0.66 to 1.14)	
DASH					0.96 (<.001)				0.98 (.049)				0.98 (.10)
Q1	10-20	131	5751.9	Referent		127	5536.3	Referent		124	5490.4	Referent	
Q2	21-23	187	9440.6	0.82 (0.66 to 1.03)		184	9062.5	0.93 (0.74 to 1.18)		180	8965.2	0.94 (0.75 to 1.19)	
Q3	24-25	119	5772.7	0.78 (0.61 to 1.00)		117	5541.5	0.96 (0.74 to 1.24)		114	5450.4	1.00 (0.77 to 1.31)	
Q4	26-27	95	4455.1	0.78 (0.60 to 1.02)		88	4240.9	0.99 (0.74 to 1.31)		87	4225.9	1.02 (0.77 to 1.36)	
Q5	28-37	123	8147.4	0.53 (0.42 to 0.68)		118	7790.2	0.76 (0.58 to 1.00)		116	7748.6	0.80 (0.61 to 1.05)	
HEI					0.98 (<.001)				0.99 (.04)				0.99 (.12)
Q1	42.1-63.2	131	6104.4	Referent		127	5841.8	Referent		124	5741.9	Referent	
Q2	63.3-69.2	131	6019.3	1.01 (0.79 to 1.28)		130	5859.8	0.85 (0.66 to 1.10)		127	5815.7	0.85 (0.66 to 1.10)	
Q3	69.3-73.9	131	6494.9	0.88 (0.69 to 1.12)		128	6241.0	0.94 (0.73 to 1.20)		124	6196.6	0.94 (0.73 to 1.22)	
Q4	74.0-79.9	131	7411.4	0.74 (0.58 to 0.94)		125	7068.9	0.77 (0.60 to 1.00)		124	7010.1	0.82 (0.63 to 1.06)	
Q5	80.0-95.4	131	7537.7	0.64 (0.51 to 0.82)		124	7160.0	0.77 (0.60 to 1.01)		122	7116.0	0.81 (0.62 to 1.06)	

[a] Adjusted for age at diagnosis and total energy. ACS = American Cancer Society nutrition guidelines score; aMED = alternate Mediterranean Diet score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension score; HEI = Healthy Eating Index score; HR = hazard ratio; PT = person-time; Q = quintile.

[b] Adjusted for age at diagnosis, total energy, race and ethnicity, education, menopausal status, physical activity, smoking, cancer stage, estrogen-receptor status, progesterone-receptor status, and HER2.

[c] Adjusted for all variables in model 2, plus body mass index, surgery type, chemotherapy, radiation, and hormonal therapies.

Table 3. Hazards ratios and 95% confidence intervals of quintiles of dietary quality indices and recurrence, breast cancer–specific death and nonbreast cancer–specific death (n = 3506)[a]

		Recurrence				Breast cancer–specific mortality				Nonbreast cancer–specific mortality			
Dietary index	Range	Events	PT, y	HR (95% CI)	HR (P_{trend})	Events	PT, y	HR (95% CI)	HR (P_{trend})	Events	PT, y	HR (95% CI)	HR (P_{trend})
ACS					1.01 (.55)				0.97 (.29)				0.94 (.03)
Q1	0-3	153	10 731.6	Referent		114	11 271.5	Referent		118	11 271.5	Referent	
Q2	4	80	5522.2	1.01 (0.77 to 1.33)		61	5746.4	1.14 (0.83 to 1.56)		63	5746.4	0.98 (0.72 to 1.34)	
Q3	5	73	5015.5	1.05 (0.79 to 1.39)		54	5211.6	1.09 (0.78 to 1.52)		44	5211.6	0.72 (0.51 to 1.02)	
Q4	6	60	4237.6	1.10 (0.81 to 1.50)		41	4425.8	1.13 (0.78 to 1.63)		52	4425.8	0.89 (0.63 to 1.25)	
Q5	7-9	83	5179.4	1.19 (0.89 to 1.57)		42	5516.2	0.75 (0.52 to 1.09)		45	5516.2	0.69 (0.48 to 0.98)	
aMED					1.02 (.46)				0.96 (.25)				0.94 (.08)
Q1	0-2	97	6688.1	Referent		75	7011.0	Referent		96	7011.0	Referent	
Q2	3	71	5188.8	1.06 (0.78 to 1.45)		56	5425.2	1.25 (0.88 to 1.79)		58	5425.2	0.83 (0.59 to 1.15)	
Q3	4	82	5533.9	1.17 (0.86 to 1.59)		60	5743.0	1.26 (0.88 to 1.80)		54	5743.0	0.80 (0.57 to 1.14)	
Q4	5	89	5081.4	1.35 (0.99 to 1.84)		62	5401.7	1.31 (0.91 to 1.90)		51	5401.7	0.91 (0.63 to 1.31)	
Q5	6-9	110	8194.0	1.08 (0.79 to 1.47)		59	8590.6	0.79 (0.54 to 1.16)		63	8590.6	0.73 (0.50 to 1.05)	
DASH					1.00 (.95)				0.99 (.68)				0.96 (.002)
Q1	10-20	75	5276.1	Referent		55	5536.3	Referent		72	5536.3	Referent	
Q2	21-23	140	8609.2	1.13 (0.85 to 1.51)		102	9062.5	1.16 (0.83 to 1.62)		82	9062.5	0.73 (0.53 to 1.00)	
Q3	24-25	74	5324.4	0.98 (0.71 to 1.37)		56	5541.5	1.03 (0.70 to 1.52)		61	5541.5	0.80 (0.56 to 1.14)	
Q4	26-27	64	4043.8	1.13 (0.80 to 1.60)		43	4240.9	1.15 (0.76 to 1.74)		45	4240.9	0.76 (0.51 to 1.12)	
Q5	28-37	96	7432.8	1.02 (0.73 to 1.41)		56	7790.2	0.93 (0.63 to 1.39)		62	7790.2	0.55 (0.38 to 0.79)	
HEI					1.01 (.30)				0.99 (.44)				0.98 (.006)
Q1	42.1-63.2	60	5630.1	Referent		49	5841.8	Referent		78	5841.8	Referent	
Q2	63.3-69.2	101	5577.1	1.39 (1.01 to 1.93)		69	5859.8	1.02 (0.70 to 1.48)		61	5859.8	0.77 (0.55 to 1.08)	
Q3	69.3-73.9	96	5948.4	1.39 (1.00 to 1.93)		72	6241.0	1.30 (0.90 to 1.88)		56	6241.0	0.67 (0.47 to 0.95)	
Q4	74.0-79.9	105	6720.9	1.33 (0.96 to 1.85)		72	7068.9	1.03 (0.71 to 1.50)		53	7068.9	0.55 (0.39 to 0.79)	
Q5	80.0-95.4	87	6809.8	1.24 (0.88 to 1.75)		50	7160.0	0.84 (0.56 to 1.27)		74	7160.0	0.67 (0.48 to 0.94)	

[a]All models adjusted for age at diagnosis, total energy, race and ethnicity, education, menopausal status, physical activity, smoking, cancer stage, estrogen-receptor status, progesterone-receptor status, and HER2. ACS = American Cancer Society nutrition guidelines score; aMED = alternate Mediterranean Diet score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension score; HEI = Healthy Eating Index score; HR = hazard ratio; PT = person-time; Q = quintile.

Table 4. Index-specific hazard ratios and 95% confidence intervals on all-cause mortality, for each component of the dietary quality index (n = 3506)[a,b]

Dietary component	ACS HR (95% CI)	aMED HR (95% CI)	DASH HR (95% CI)	HEI HR (95% CI)
Fruits				
Total fruit	—	1.02 (0.86 to 1.21)	1.03 (0.96 to 1.10)	1.12 (1.02 to 1.23)
Whole fruits	—	—	—	0.94 (0.85 to 1.04)
Vegetables				
Total vegetables	—	0.97 (0.81 to 1.16)	1.01 (0.94 to 1.08)	1.06 (0.92 to 1.23)
Greens and beans	—	—	—	0.92 (0.83 to 1.02)
Total fruits and vegetables	0.98 (0.91 to 1.06)	—	—	—
Grains				
Whole grains	0.91 (0.85 to 0.99)	0.92 (0.77 to 1.09)	0.96 (0.90 to 1.02)	0.98 (0.96 to 1.01)
Refined grains	—	—	—	0.95 (0.90 to 0.99)
Dairy				
Total dairy	—	—	—	1.00 (0.96 to 1.03)
Low-fat dairy	—	—	0.95 (0.89 to 1.00)	—
Protein foods				
Total protein foods	—	—	—	1.02 (0.91 to 1.14)
Seafood and plant proteins	—	—	—	1.01 (0.92 to 1.11)
Red and processed meats	0.99 (0.91 to 1.08)	0.96 (0.80 to 1.15)	1.02 (0.95 to 1.10)	—
Fish	—	1.08 (0.91 to 1.28)	—	—
Legumes	—	0.95 (0.80 to 1.14)	—	—
Nuts	—	0.82 (0.68 to 0.98)	—	—
Nuts and legumes	—	—	0.93 (0.87 to 1.00)	—
Fat				
Unsaturated fats	—	1.01 (0.85 to 1.19)	—	1.02 (0.98 to 1.06)
Saturated fats	—	—	—	0.98 (0.94 to 1.02)
Sodium	—	—	0.93 (0.82 to 1.04)	0.96 (0.92 to 0.99)
Sugar				
Added sugar	—	—	—	0.96 (0.92 to 1.01)
Sweetened beverages	—	—	0.98 (0.92 to 1.04)	—
Alcohol	—	0.99 (0.79 to 1.25)	—	—

[a]All models adjusted for age at diagnosis, total energy, race and ethnicity, education, menopausal status, physical activity, smoking, cancer stage, estrogen-receptor status, progesterone-receptor status, HER2, and all other components within the index. — = Not Applicable; ACS = American Cancer Society nutrition guidelines score; aMED = alternate Mediterranean Diet score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension score; HEI = Healthy Eating Index score; HR = hazard ratio.

[b]All hazard ratios calculated as a 1-unit change within the dietary quality index component-specific score.

95% CI = 0.85 to 0.99) and nuts in the case of aMED (HR = 0.82, 95% CI = 0.68 to 0.98) were each associated with a lower risk of all-cause mortality. In the case of HEI and all-cause mortality, a decreased intake of refined grains (HR = 0.95, 95% CI = 0.90 to 0.99) and sodium (HR = 0.96, 95% CI = 0.92 to 0.99) were each associated with lower risk, and higher intake of total fruit (HR = 1.12, 95% CI = 1.02 to 1.23) was associated with higher risk.

Examination of the interaction between the dietary quality indices and ER on all-cause mortality suggested a stronger association among patients with ER-positive breast cancer when comparing the highest to lowest quartile for each of the dietary quality index scores. For example, for women with ER-positive breast cancer, the hazard ratio comparing highest to lowest ACS categories was 0.68 (95% CI = 0.51 to 0.91), whereas for women with ER-negative breast cancer, it was 1.05 (95% CI = 0.59 to 1.89). The *P* values for the interaction terms were not statistically significant (Table 5). No statistically significant interactions were observed when evaluating the dietary quality indices by each of PR, HER2, chemotherapy, and radiation therapy.

Discussion

In this prospective cohort study of 3660 breast cancer survivors, participants who reported consuming diets that were more concordant with healthy eating patterns, as measured by 4 major dietary quality indices, were at lower risk of nonbreast cancer–specific and all-cause mortality. No clear patterns emerged when examining the associations between the dietary quality indices and breast cancer recurrence or breast cancer–specific mortality.

The ACS, aMED, DASH, and HEI were each associated with a lower risk for all-cause mortality when comparing the highest to lowest categories and adjusting for all variables in model 2. These results are consistent with the findings from the SBCSS (15), in that they found a 34% lower risk of all-cause mortality when comparing extreme quartiles of DASH among breast cancer survivors at 5 years postdiagnosis. However, they did not report statistically significant associations in their assessment of HEI (15). One reason for this may be that HEI was developed to correspond to the recommendations of the US dietary guidelines, and these guidelines may not be as directly applicable to dietary patterns in Shanghai.

The ACS, aMED, DASH, and HEI were each associated with a lower risk for nonbreast cancer–specific mortality, whereas none were associated with breast cancer–specific outcomes. Our findings are consistent with prior literature (11,12,30), with the exception of SBCSS, which reported an association between DASH and breast cancer–specific events (15). One explanation

Table 5. Hazards ratios and 95% confidence intervals of quintiles of dietary quality indices and all-cause mortality, stratified by ER status[a]

		ER positive (n = 2942)				ER negative (n = 564)				
Dietary index	Range	Events	PT, y	HR (95% CI)	HR (P_{trend})	Events	PT, y	HR (95% CI)	HR (P_{trend})	$P_{interaction}$
ACS					0.94 (.01)				1.02 (.63)	.24
Q1	0-3	194	9554.9	Referent		38	1716.6	Referent		
Q2	4	90	4892.3	0.87 (0.68 to 1.13)		34	854.1	1.74 (1.07 to 2.83)		
Q3	5	77	4402.2	0.83 (0.64 to 1.09)		21	809.5	1.29 (0.75 to 2.22)		
Q4	6	74	3804.1	0.90 (0.68 to 1.19)		19	621.7	1.55 (0.85 to 2.83)		
Q5	7-9	67	4626.8	0.68 (0.51 to 0.91)		20	889.4	1.05 (0.59 to 1.89)		
aMED					0.95 (.08)				0.98 (.72)	.17
Q1	0-2	141	5727.4	Referent		30	1283.6	Referent		
Q2	3	85	4703.4	0.91 (0.69 to 1.20)		29	721.7	1.55 (0.91 to 2.63)		
Q3	4	96	4863.2	0.99 (0.75 to 1.30)		18	879.8	1.04 (0.56 to 1.92)		
Q4	5	84	4618.7	0.95 (0.71 to 1.26)		29	783	1.92 (1.07 to 3.44)		
Q5	6-9	96	7367.6	0.75 (0.56 to 1.01)		26	1223	0.92 (0.49 to 1.71)		
DASH					0.98 (.02)				1.01 (.55)	.08
Q1	10-20	107	4615.9	Referent		20	920.4	Referent		
Q2	21-23	140	7575.2	0.89 (0.69 to 1.15)		44	1487.3	1.33 (0.77 to 2.32)		
Q3	24-25	96	4789	0.89 (0.67 to 1.19)		21	752.5	1.36 (0.71 to 2.60)		
Q4	26-27	65	3577.5	0.91 (0.66 to 1.26)		23	663.4	1.60 (0.84 to 3.04)		
Q5	28-37	94	6722.7	0.70 (0.52 to 0.95)		24	1067.5	1.25 (0.64 to 2.43)		
HEI					0.99 (.03)				1.00 (.99)	.32
Q1	42.1-63.2	104	5044.3	Referent		23	797.6	Referent		
Q2	63.3-69.2	101	4786.9	0.91 (0.69 to 1.21)		29	1072.9	0.71 (0.40 to 1.24)		
Q3	69.3-73.9	102	5297.3	1.00 (0.76 to 1.32)		26	943.7	0.85 (0.48 to 1.52)		
Q4	74.0-79.9	90	5966.2	0.72 (0.54 to 0.97)		35	1102.7	1.06 (0.61 to 1.83)		
Q5	80.0-95.4	105	6185.6	0.80 (0.60 to 1.06)		19	974.3	0.73 (0.38 to 1.40)		

[a]All models adjusted for age at diagnosis, total energy, race and ethnicity, education, menopausal status, physical activity, smoking, cancer stage, estrogen-receptor status, progesterone-receptor status, and HER2. ACS = American Cancer Society nutrition guidelines score; aMED = alternate Mediterranean Diet score; CI = confidence interval; DASH = Dietary Approaches to Stop Hypertension score; ER = estrogen receptor; HEI = Healthy Eating Index score; HR = hazard ratio; PT = person-time; Q = quintile.

for our findings could be related to diet quality playing a more important role in cardiovascular disease (CVD) than on breast cancer prognosis and women surviving breast cancer being at greater risk for CVD as compared with women without breast cancer (31). One prior study found breast cancer patients to be at higher risk of dying from CVD than from their breast cancer at 10 years after diagnosis (32), which could be explained by cardiotoxic cancer treatments and exacerbated by associated CVD risk factors (33,34).

The correlation coefficients comparing each of the dietary quality indices suggest some overlap in their assessment of diet; however, each appears to have some independent characteristics (Supplementary Table 3, available online). To investigate the main drivers of each index, we explored the associations of the individual dietary component scores on all-cause mortality while adjusting for the other dietary components within each index. We found independent associations with all-cause mortality for whole grains in the case of ACS and nuts in the case of aMED. Interestingly, these findings are consistent with prior research on the impact of these individual food items and breast cancer incidence (35,36).

The adjusted interaction between each of the 4 dietary quality indices and ER on all-cause mortality suggested a stronger association among patients with ER-positive breast cancer when comparing the highest to lowest quartile of the dietary quality index score. However, the P values for the interaction terms were not statistically significant. These findings are consistent with 1 prior study (11) and may be because ER-positive survivors generally having a better prognosis as compared with those who are ER negative and therefore more likely to die of other causes (32). For these ER-positive patients, diet quality may have had a stronger impact on causes of death other than breast cancer.

There are several strengths to this study, including drawing from a large population of women newly diagnosed with breast cancer, prospective data collection with a long follow-up period, and comprehensive measures of dietary exposures, outcomes, and covariates. The main limitations of this study are the use of a single dietary measure at baseline and not addressing dietary changes that could occur after that point; our population being predominantly White and therefore underpowered to examine differences by race and ethnicity; and apart from HEI, the associations of each of the dietary quality indices being restricted to the highest quintile when comparing with the lowest, suggesting that participants in the highest group could have some unidentified behaviors that are not accounted for in the analysis. Finally, it is always possible that participants who chose to enroll in this study were systematically different than those who did not. However, when comparing the enrolled with the unenrolled, the differences in age, race, ethnicity, BMI, and cancer stage were minimal.

In summary, our study found that the ACS, aMED, DASH, and HEI were each associated with a decreased risk of nonbreast cancer–specific and all-cause mortality. However, the dietary quality indices were not associated with breast cancer–specific outcomes. These findings highlight the importance of an overall healthy dietary pattern for breast cancer survivors.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author (IJE). The data are not publicly available due to their containing protected health information that could compromise the privacy of research participants.

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