Journal Pre-proof

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PII: S1526-8209(21)00198-1
DOI: https://doi.org/10.1016/j.clbc.2021.07.010
Reference: CLBC 1351

To appear in: *Clinical Breast Cancer*

Received date: Mar 6, 2021
Revised date: Jun 15, 2021
Accepted date: Jul 20, 2021

Please cite this article as: Fatemeh Toorang , Bahareh Sasanfar , Ahmad Esmaillzadeh , Kazem Zendehdel , Adherence to the DASH Diet and Risk of Breast Cancer, *Clinical Breast Cancer* (2021), doi: https://doi.org/10.1016/j.clbc.2021.07.010

Adherence to the DASH Diet and Risk of Breast Cancer

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Running title: DASH diet and breast cancer

Abstract word count: 350

Text word count: 4290

Number of Tables: 3

Number of Figures: 0

Acknowledgments: We are grateful to Maryam Mousavi for assistance with data cleaning, and Vahideh Peyghambari who supervised data gathering.

Statement of authorship:

FT and KZ designed the study, BS supervised data collection and data cleaning. FT analyzed the data and drafted the manuscript. AE guided the drafting of the manuscript and revised the final edition. All authors approved the final version of the manuscript.

Disclosure statement

None of the authors declared any conflicts of interest.

Funding

This study was supported by a fund from the Cancer Research Center, Tehran University of Medical Sciences (no.93-03-51-27113).

Ethics: Face-to-face description of the study aims and protocol were provided to each participant before signing the written informed consent form. The study protocol was approved by the ethical committee of the Cancer Research Center, Tehran University of Medical Sciences (no. 93-03-51-27113).

ABSTRACT:

Background& Purpose: The Dietary Approach to Stop Hypertension (DASH) eating pattern has been recommended as a healthy dietary plan by several international guidelines. However, data on the association between the DASH diet and breast cancer is limited. This study investigated the association between the DASH dietary pattern and risk of breast cancer.

Methods: This is a hospital-based case-control study conducted between 2014 and 2016 in the Cancer Institute of Iran. Patients with histopathologically confirmed breast cancer were recruited. Controls were healthy subjects who were frequency matched to cases by residential place and age (±10years). A validated 168-item Food Frequency Questionnaire (FFQ) was applied to assess the dietary intake of participants. Physical activity was assessed using the Global Physical Activity Questionnaire (GPAQ). The DASH dietary pattern scores were calculated using the method introduced by Fung. Unconditional logistic regression, in which potential confounders were taken into account, was applied to determine the association between adherence to the DASH dietary pattern and odds of breast cancer.

Results: The study participants comprised 477 patients with breast cancer and 507 healthy controls. In the total population, patients with breast cancer were slightly older (45.9 vs. 43.9 y, P=0.02), had slightly higher BMI (21.9 vs. 20.2, P=0.01) and were less physically active (20 vs. 27 MET h/wk. P<0.01) than controls. In Model A, which was adjusted for age and energy intake, adherence to the DASH dietary pattern substantially reduced breast cancer risk in the total population (OR for comparing extreme tertiles: 0.62; 95% CI 0.44-0.78; P_{trend} =0.004). Even after controlling for more cofounders, greatest adherence to DASH diet was associated with a 34% reduction in risk of breast cancer (OR 0.66; 95% CI 0.46, 0.94; P_{trend}=0.03). In premenopausal women, adherence to the DASH dietary pattern was

insignificantly associated with a 32% reduction in breast cancer risk. This risk reduction was 38% in postmenopausal women, which was also not found to be significant

Conclusion: Adherence to the DASH dietary pattern could be associated with an approximately 30% reduction in risk of breast cancer. However, further studies, in particular studies with prospective design, are required to confirm this claim.

INTRODUCTION

Breast cancer is the most common cancer among women worldwide. It was recognized as the fifth cause of cancer death both in low- and high-income countries. The GLOBOCAN report demonstrated that breast cancer is increasing all over the world; around 1.38 million new cases of breast cancer were diagnosed in 2008, increasing to 1.67 million in 2012(1-3). Although its incidence rates are lower in most Asian countries than countries of the West, its incidence and mortality rate have risen substantially in most Asian areas (3-5).

Breast cancer is reported as the most prevalent cancer in Iran, with an ASR of 33.21 in 100.000 people (6). Like most Asian countries, breast cancer mortality happens in a younger age in Iran than high-income countries, with the mean age being 49.8 years in Iran (6-8). This increases the social and economic cost of breast cancer in these countries and emphasizes the importance of prevention and early detection of breast cancer in this area(7). It is clear that the first step of prevention is clarifying the associated risk factors.

Dietary factors have been mostly studied as a modifiable risk factor for breast cancer alongside obesity (in post-menopausal women), physical inactivity, alcohol consumption and reproductive and hormonal factors (3, 9). Migration studies demonstrate that differences in dietary intake may play an important role in international variations in breast cancer incidence (4). However, the association between dietary habits and breast cancer remained inconclusive in most aspects (9). Most studies have investigated the association between individual nutrient or food intake and risk of breast cancer with inclusive results (10) . Studies in this approach are valuable, however it is important to note that foods are eaten together and they have synergistic or antagonistic effects on each other. Therefore, dietary patterns are a more reliable approach in diet and diseases studies (11, 12). Moreover,

investigating the association between dietary patterns and risk of cancer could help in devising more comprehensible dietary guidelines.

The Dietary Approach to Stop Hypertension (DASH) diet is a dietary pattern initially recommended for management of hypertension(13) . It is high in fruits, vegetables, legumes and nuts which provide substantial amounts of plant proteins. It emphasizes whole grain, fruits and vegetables and minimizes the consumption of sodium, sweetened beverages and red and processed meats and recommends a medium amount of low-fat dairy (13). Favorable effects of this diet on metabolic syndrome (14, 15), diabetes (16) and cardiovascular diseases (17) have been suggested. This dietary pattern may have relevance to cancer prevention, particularly because it is highly similar to cancer prevention guidelines created by the American Cancer Society and World Cancer Research Fund (18, 19). Several studies including systematic reviews showed that higher intake of fruit, vegetable , whole grain and legumes and lower intake of red and processed meats and simple carbohydrate which is highly similar to DASH dietary pattern, is inversely associated with risk of breast cancer (20-23). Several studies have investigated the association between the DASH diet and different type of cancers (24-26). However, these studies have been mostly focused on colorectal cancer (24-26). Data on the association between this dietary pattern and risk of breast cancer are insufficient, with inconclusive results(26). Furthermore, these studies were mainly conducted in the USA and there are hardly any studies in low- or middle-income countries. Moreover, a systematic review of all studies on breast cancer and nutrition by world cancer research fund, concluded that there is limited data on the association between dietary intakes and food patterns with risk of post or pre-menopause breast cancers(19). This report concurred that more studies are needed and recommended the association would be different in post and pre-menopause groups(19).

Iranian household mainly consume an unhealthy diet which is fairly different from DASHdiet. Their diet is low in fruits, vegetables and dairy product (27). These unhealthy dietary habits are common in Iranian women especially from lower socioeconomic status (28). however, their intake of meat products is extremely lower than western countries(27). A review on nutrition and breast cancer in Middle East reviled that breast cancer risk factors are probably different in this area and needs more investigations (29). Middle Eastern societies such as the Iranian population consume a diet high in grains and low in animal foods, which is different from both western and eastern countries (29-32). Also, drinking alcohol and smoking, both of which are considered major risk factors of breast cancer, are not commonplace in women of these countries (33, 34). Therefore, the effect of dietary patterns in this population could be dissimilar to other regions. Hence, this study investigated the association between the DASH diet and risk of breast cancer in a hospital-based case-control study in Iranian women.

MATERIALS/ SUBJECTS and METHODS

Participants: This was a hospital-based case-control study conducted between 2014 and 2016 in the Cancer Institute of Iran, located at Imam Khomeini Hospital Complex in Tehran. Patients (n=486) with histopathologically confirmed breast cancer were recruited. Patients were aged 19-80 years and had received a cancer diagnosis in the previous year, with no previous history of other cancers. Healthy subjects who come to visit their relatives in the same hospital and had no long-term dietary restrictions were recruited as controls. Controls (523) were frequency-matched to cases by residential place and age (±10years).

Assessment of Dietary Intake: We used a validated 168-item Food Frequency Questionnaire (FFQ) to assess the dietary intake of participants. A detailed description of this FFQ, including its development and validity has been provided elsewhere (35). Briefly, it was a

willet FFQ including 168 questions related to intake of food items with standard portion sizes within the past 12 months. The participants were asked to recall their food intake in the preceding year through a face-to-face interview conducted by trained nutritionists. Patients with breast cancer were asked to recall their food consumption prior to the appearance of cancer. Data was converted to daily intake, after which intake of energy and nutrients were computed using the USDA food composition table. Subjects who didn't answer to more than 70 items of the FFQ (n=25, 9 patients and 25 controls) were excluded. Further description of this study is reported elsewhere(36).

Adherence to the DASH diet: The DASH dietary pattern scores were calculated using the method introduced by Fung(37). To investigate subjects' adherence to the DASH diet, we initially calculated energy-adjusted intake of food and nutrients using a residual method suggested by willet (38). Participants were then categorized into quintiles of energy-adjusted foods and nutrients intake .The highest scores were allocated to individuals in the highest quintile of grains, vegetables, fruits, low-fat dairies, legumes and nuts. Clearly, the lowest quintiles of intake in these food groups received the lowest scores. Opposite scores were allocated to food groups or nutrients minimized in the DASH diet such as red and processed meats, sweetened beverages, sweets, and sodium intake. Finally, the total DASH score was calculated by summing up the score of the eight components for each person. The DASH scores could therefore range from 8 to 40.

Assessment of Breast Cancer: Diagnosis of breast cancer was made based on biopsy samples reviewed by an experienced pathologist. Patients with histopathologically confirmed breast cancer (as defined by the second edition of the International Classification of Diseases for Oncology (ICDO-C50.0-C50.9). were enrolled. It should be mentioned that, only patients

who had been diagnosed within one year prior to the date of the interview were recruited in the study.

Assessment of Covariates: Physical activity was assessed using the Global Physical Activity Questionnaire (GPAQ) which is a famous validated tool (39). BMI was calculated using the weight and height of participants which were measured based on standard protocol. Demographic information and data on other risk factors of breast cancer were obtained using a structured questionnaire through a face-to-face interview conducted by health bachelors.

Statistical Analysis: Characteristics of patients with breast cancer and controls were compared using student's independent t test for continuous variables and chi-square test for categorical variables. Unconditional logistic regression models were used to determine the association between adherence to the DASH diet and odds of breast cancer. In these analyses, we first controlled for age (continuous) and energy intake (continuous) in model A. In model B, additional adjustments were made for education (literate, illiterate), alcohol intake (yes or no), smoking status (yes, no), physical activity (MET h/week), family history of breast cancer (yes, no), marital status (single, married), oral contraceptive use (yes, no), parity (number of children), fertility treatment (using drugs or other measures to increase pregnancy chances) (yes, no) and BMI (continuous). In all these analyses, the first tertile of the DASH diet score was considered as a reference and the odds ratios (ORs) and 95% CIs for breast cancer were reported. The trend of odds ratios was examined by considering the DASH diet tertiles as a continuous variable. All statistical analyses were carried out using STATA (STATA, version 14, State Corp., College station, TX).

RESULTS

Study participants comprised 477 patients with breast cancer and 507 healthy controls. Table 1 shows the distribution of patients and controls in pre-menopausal and post-menopausal

subjects and overall, according to selected covariates. In the whole study population, patients with breast cancer were slightly older (45.9 vs. 43.9 y, P=0.02), had slightly higher BMI at 30 years of age (21.9 vs. 20.2, P=0.01) and were less physically active (20 vs. 27 MET h/wk. P<0.01) than controls. Patients were less likely to use post-menopausal hormones (2 vs. 10%, P=0.03) or drink alcohol (6.3 vs. 2.5%, P<0.01) than controls. A family history of breast cancer was more common in patients overall (46 vs. 7%, P<0.001).

In pre-menopausal subjects, patients with breast cancer were slightly older (41.2 vs. 39.5 y, P<0.01) and were less physically active (20.3 vs. 28.2 MET h/wk. P<0.01) than controls. Pre-menopausal breast cancer patients drank alcohol less frequently (9 vs. 19%, P<0.05) and were more likely to have had a history of breast cancer in their relatives (30 vs. 4 %, P<0.001) compared to controls.

When examining the general characteristics of post-menopausal subjects, we found no difference in the prevalence of covariates except for family history of breast cancer which was higher in patients (16 vs. 3 %, P<0.01) and oral contraceptive use (44 vs. 57 %, P=0.02) and number of children (3.2 vs. 3.7 n, P=0.02) which were lower in patients compared to controls.

Intake of the DASH dietary pattern components in participants is shown in Table 2. Compared to controls, patients with breast cancer had significantly lower intake of vegetables (309 vs. 346 g/d, P<0.01) in the total sample. This was also observed in pre-menopausal subjects, with patients eating less vegetables than controls (305 vs. 352, P<0.01). The energy intake of patients was slightly higher in this group (3127 vs. 2866 kcal/d, P=0.2). Patients ate less grain than controls in post-menopausal subjects (428 vs. 470 g/d, P=0.03).

Multivariable adjusted ORs for breast cancer across the tertiles of DASH diet score in these three groups are provided in **Table 3**. In the total study population, it was found that

adherence to the DASH dietary pattern substantially reduced breast cancer risk in model A which was adjusted for age and energy intake (OR for comparing extreme tertiles: 0.62; 95% CI 0.44-0.78; P_{trend} =0.004). Even after additional controlling for education (literate, illiterate), smoking (yes, no), alcohol intake (yes, no), physical activity (MET h/wk.), family history of breast cancer (yes, no), marital status (married/single), oral contraceptive use (yes, no), parity (number of children), fertility treatment (yes, no), hormone replace therapy (yes, no) and BMI (kg/m^2), greatest adherence to the DASH diet was associated with a 34% reduction in risk of gastric cancer (OR 0.66; 95% CI 0.46, 0.94; P_{trend}=0.03).

In pre-menopausal women, adherence to the DASH dietary pattern was associated with a 32% reduction in breast cancer risk. This association was attenuated after adjusting for covariates and it was not found to be significant in either of the models. A similar trend was found in post-menopausal women. No significant association was shown in model A (OR 0.62; 95% CI 0.34, 1.1; P_{trend}=0.09) and this did not change considerably after adjusting for different covariates.

DISCUSSION

In this large hospital-based case-control study, we found a strong association between adherence to the DASH dietary pattern and odds of breast cancer. This dietary pattern was associated with a 34% reduction in breast cancer risk in the total study group. The risk reduction was 32% in premenopausal women, and 38% reduction in postmenopausal women, although the association was not found to be significant in these subgroups.

A few studies have investigated the association between this dietary pattern and risk of breast cancer, with inconclusive results (40, 41). Studies mainly showed a protective effect of the DASH diet on risk of breast cancer in post-menopausal women or receptor-negative breast cancer(40). The genetic factors and early life events are more important in pre-menopausal

breast cancer development and life style factors including dietary habits could be more important in postmenopausal women which could be partly described through the effects of dietary components on insulin and estrogen levels (42, 43). However, several studies showed significant associations between the various components of the DASH dietary pattern and risk of breast cancer. For instance, several studies indicated that high intake of red and processed meats could increase breast cancer risk(44, 45). Fruits, vegetables and dairy are the most emphasized components of this dietary pattern and several studies have reported their protective effects on breast cancer(46). However, the comprehensive review on nutrition and breast cancer prevention published by the World Cancer Research Fund revealed that the evidence on the association between foods or nutrients and risk of breast cancer is not convincing (19, 47). This report asserted that there is limited evidence on the negative association between the risk of post- and pre-menopausal breast cancer with intake of non-starchy vegetables and food containing carotenes and a high-calcium diet. Evidence on other dietary factors has been classified as inconclusive.

Several theories have been suggested as mechanisms of the association between the DASH dietary pattern and risk of cancers. The DASH dietary pattern emphasizes high intake of fruits, vegetables, dairy, whole grains, legumes and nuts. On the other hand, low consumption of sweetened beverages and red and processed meats might further explain the reduction of breast cancer risk in individuals who follow this dietary pattern(47). This diet is high in dietary fiber, calcium, folate, carotenes and phenolic compounds(48). The association of these nutrients with breast cancer risk has been suggested in several studies (49-52). Furthermore, this dietary pattern is high in dietary antioxidants such as pro-anthocyanidines, flavonoids, stilbenes and alpha-tocopherols (48, 53) which could reduce cancer risk(54-56). Moreover, it is associated with lower circulating C-reactive protein which could explain the anti-inflammatory effect of this diet(57, 58). Decreased inflammation and enhanced

antioxidant capacity of the body could suppress cell proliferation, spontaneous mutation and DNA methylation, all of which may lead to reduced cancer incidence.(56, 59)

The DASH dietary pattern insists on higher intake of fiber and lower intake of simple carbohydrates, both of which are associated with lower glycemic index. It could therefore decrease the circulating level of insulin and insulin-like growth factor 1, which are associated with an elevated risk of ontogenesis (60, 61). Several studies have suggested a greater risk of breast cancer in hyperinsulinemia and diabetic patients (62, 63). Besides, higher intake of fiber may decrease circulating androstenedione and estrogen levels which indirectly diminish the risk of breast cancer(64, 65).

The DASH dietary pattern emphasizes consumption of low-fat dairy products which have been associated with lower risk of breast cancer in several studies(66). It has been proposed that calcium has anti-proliferation, pro-apoptotic and pro-differentiation effects on mammary gland cells (67, 68). Furthermore, conjugated linoleic acid (CLA) - a component in dairy products- has several anti-cancer capacities. It has been shown to inhibit cell proliferation, suppress production of inflammatory substances and empower immune responses(69, 70).

Use of a valid and reproducible FFQ for dietary assessment, similarities in the socioeconomic status of patients and controls, controlling for several confounders and stratified analysis based on menopausal status could be mentioned as some of the strengths of this study. However, there are some limitations. First, a medium sample size limited us in finding significant associations in our subgroup analyses, since the sample sizes in quartiles of pre- and post- menopausal subjects were too small for us to find a significant association. Although we controlled for several confounders, the possibility of residual confounding and recall bias cannot be excluded in case-control studies(71). Moreover, we should mention the possibility of misclassification of study participants based on their dietary intake which is a

common problem in all epidemiological studies that use FFQ(71). In order to reduce the possibility of misclassification, we applied energy-adjusted intake of food groups in order to compute adherence to the DASH dietary pattern(38). One of the weak points in our approach in scoring individual adherence to the DASH dietary pattern is attributing equal weight to all food groups, while some food groups might have greater effects than others on breast cancer development.

On the basis of this case-control study, it appears that adherence to DASH dietary pattern was associated with around 30% reduction in risk of breast cancer. This finding is in accordance with the current recommendations by World Cancer Research fund International (WCRC), American Cancer Society and International Agency for Research on Cancer (IARC) which emphasize consuming high amounts of plant-based foods in a person's daily diet. Although several systematic reviews concurred that there is not sufficient data to make a definite recommendation on proper diet to breast cancer prevention, the dash diet could reduce risk of several health events and possibly reduce risk of breast cancer, therefore, it could be recommended as a strategy for healthier life and probably breast cancer prevention. However, larger studies, in particular studies with a prospective design, are required to confirm the association between dietary patterns and risk of breast cancer, particularly in post- or pre-menopausal women.

Table1. Characteristics of the cases and controls recruited to study adherence to the DASH diet and risk of breast cancer by menopausal status [1]

Characteristics	Total			Pre-menopause			Post-menopause		
	Cases (n=477)	Controls (n=507)	P[2]	Cases (n=313)	Controls (n=308)	P[2]	Cases (n=156)	Controls (n=161)	P[2]
DASH score (mean)	23.6	24.3	0.02	24	25	0.05	24	24	0.13
Age (years)	45.9±10.3	43.9±11.2	<0.01	41.2±7.3	39.5±8.3	<0.01	55.4±8.7	53.9±9.3	0.15
BMI (kg/m^2)	28.1±5.1	28.9±5.6	0.02	27.6±4.9	28.8±5.7	<0.01	29.1±5.3	30.0±5.3	0.11
BMI at age 30 (kg/m^2)	21.9±8.8	20.2±11.4	0.01	21.9±8.9	20.6±11.5	0.12	21.8±8.4	20.4±10.8	0.24
Physical activity (MET h/wk.)	20.0±38.5	27.0±38.5	<0.01	20.3±25.9	28.2±37.8	<0.01	20.2±24.8	27.7±42.2	0.06
Education (literate, n, %)	416(87)	460(91)	0.08	293(94)	290(94)	0.78	116(74)	133(83)	0.07
Marital status (Married, n,%)	448(94)	479(94)	0.71	290(93)	294(96)	0.14	152(97)	159(99)	0.39
Smoking (yes, n, %)	18(3)	27(5)	0.24	10(3)	8(3)	0.66	8(5)	16(10)	0.11
Drinking Alcohol (yes, n, %)	12(2.5)	31(6)	<0.01	9(3)	19(6)	0.04	3(2)	9(6)	0.09
Family history of breast cancer (yes, n, %)	46(10)	7(1)	<0.001	30(10)	4(1)	<0.001	16(10)	3(2)	<0.01
Oral contraceptive use (yes, n, %)	227(48)	263(52)	0.18	154(49)	159(52)	0.57	69(44)	92(57)	0.02
Parity (number of children)	2.4±1.7	2.5±1.9	0.54	2.1±1.4	2.1±1.4	0.78	3.2±2.8	3.7±3.4	0.02
Hormone replacement therapy (yes, n, %)	2(0.4)	10(2)	0.03	0(0)	2(0.65)	0.15	2(1)	7(4)	0.1
Fertility treatment ((yes, n, %)	19(3.9)	30(6)	0.18	10(3)	19(6)		9(6)	9(6)	0.95

[1] reported figures are mean± SDs unless indicated

[2] obtained from independent' s t-test for continuous variables and chi-square test for categorical variables

Table 2. Dietary intake across participants in study of adherence to the DASH diet and risk of breast cancer overall and by menopausal status[1]

Food Group / Nutrient	Total			Pre-menopause			Post-menopause		
	Cases (n=477)	Controls (n=507)	P[2]	Cases (n=3013)	Controls (n=308)	P[2]	Cases (n=156)	Controls (n=161)	P[2]
Energy (kcal/d)	2965±1433	2965±1433	0.97	3127±1527	2866±1251	0.02	2633±92	2674±89	0.75
Grains (g/d)	450±207	448±207	0.05	463±214	436±223	0.12	428±170	470±173	0.03
Nuts and legumes (g/d)	56±49	60±67	0.13	54±43	62±78	0.13	59±59	57±48	0.75
Vegetables (g/d)	309±231	364±208	<0.01	305±217	352±221	<0.01	324±254	332±180	0.75
Fruits (g/d)	577±391	602±375	0.15	570±22	611±23	0.20	595±30	585±27	0.80
Low-fat dairy (g/d)	57±123	68±151	0.09	57±7	69±8	0.26	55±131	71±172	0.35
Red and processed meats (g/d)	20±23	20±22	0.36	20±21	20±25	0.83	20±28	20±14	0.78
Sweetened beverages(g/d)	100±170	90±6	0.85	100±176	90±115	0.47	103±156	87±156	0.36
Sodium (g/d)	1984±69	2115±84	0.11	1956±1313	2148±2273	0.20	1994±1731	2107±104	0.48

[1] reported figures are mean± SDs

[2] obtained from independent' s t-test

Table3. Odd Ratios (ORs) and 95% Confidence Intervals (CIs) for breast cancer across tertiles of DASH score

	OR(95%CI)			
	Tertile 1	Tertile 2	Tertile 3	P_{trend} [1]
Total				
No. of cases/ controls (477/507)	183/156	186/211	140/108	
Model A[2]	1	0.76(0.57-1.02)	0.62(0.44-0.87)	0.004
Model B[3]	1	0.78(0.58-1.07)	0.66(0.46-0.94)	0.03
Pre-menopause				
No. of cases/ controls (313/308)	113/94	127/129	73/85	
Model A[2]	1	0.84(0.58-1.22)	0.68(0.46-1.22)	0.07
Model B[3]	1	0.92(0.62-1.37)	0.78(0.50-1.23)	0.29
Post-menopause				
No. of cases/ controls (156/161)	64/51	61/69	31/41	
Model A[2]	1	0.69(0.42-1.2)	0.62(0.34-1.1)	0.09
Model B[3]	1	0.69(0.40-1.2)	0.66(0.35-1.2)	0.17

[1]Trend based on median value of each tertile

[2]Adjusted for age and energy intake

[3]Further adjusted for education (literate, illiterate), smoking (yes, no), alcohol intake (yes, no), physical activity (MET h/wk.), family history of breast cancer (yes, no), marital status (married/single), oral contraceptive use (yes, no), parity (number of children), fertility treatment (yes, no), hormone replace therapy (yes, no), BMI (kg/m^2)

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International journal of cancer. 2010;127(12):2893-917.
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International journal of cancer. 2015;136(5).
3. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. Cancer Epidemiology and Prevention Biomarkers. 2016;25(1):16-27.
4. Kojima R, Okada E, Ukawa S, Mori M, Wakai K, Date C, et al. Dietary patterns and breast cancer risk in a prospective Japanese study. Breast cancer. 2017;24(1):152-60.
5. Huang C-S, Lin C-H, Lu Y-S, Shen C-Y. Unique features of breast cancer in Asian women—breast cancer in Taiwan as an example. The Journal of steroid biochemistry and molecular biology. 2010;118(4-5):300-3.
6. Nafissi N, Khayamzadeh M, Zeinali Z, Mohammadi G, Hosseini M, Akbari M. Breast Cancer in Iran, from Epidemiology, Clinicopathological and Biomarker Feature. Advances in Bioresearch. 2017;8(2).
7. Daroudi R, Sari AA, Nahvijou A, Kalaghchi B, Najafi M, Zendehdel K. The economic burden of breast cancer in Iran. Iranian journal of public health. 2015;44(9):1225.
8. Ghiasvand R, Adami H-O, Harirchi I, Akrami R, Zendehdel K. Higher incidence of premenopausal breast cancer in less developed countries; myth or truth? BMC cancer. 2014;14(1):343.
9. Gong Z, Ambrosone CB, McCann SE, Zirpoli G, Chandran U, Hong CC, et al. Associations of dietary folate, Vitamins B6 and B12 and methionine intake with risk of breast cancer among African American and European American women. International journal of cancer. 2014;134(6):1422-35.
10. Mourouti N, Kontogianni MD, Papavagelis C, Panagiotakos DB. Diet and breast cancer: a systematic review. International journal of food sciences and nutrition. 2015;66(1):1-42.
11. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Current opinion in lipidology. 2002;13(1):3-9.
12. Kant AK. Dietary patterns and health outcomes. Journal of the American Dietetic Association. 2004;104(4):615-35.
13. Sacks FM, Obarzanek E, Windhauser MM, Svetkey LP, Vollmer WM, McCullough M, et al. Rationale and design of the Dietary Approaches to Stop Hypertension trial (DASH): a multicenter controlled-feeding study of dietary patterns to lower blood pressure. Annals of epidemiology. 1995;5(2):108-18.
14. Asghari G, Yuzbashian E, Mirmiran P, Hooshmand F, Najafi R, Azizi F. Dietary approaches to stop hypertension (DASH) dietary pattern is associated with reduced incidence of metabolic syndrome in children and adolescents. The Journal of pediatrics. 2016;174:178-84. e1.
15. Park Y-MM, Steck SE, Fung TT, Zhang J, Hazlett LJ, Han K, et al. Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) style diet, and metabolic health in US adults. Clinical Nutrition. 2017;36(5):1301-9.
16. Jannasch F, Kröger J, Schulze MB. Dietary Patterns and Type 2 Diabetes: A Systematic Literature Review and Meta-Analysis of Prospective Studies–3. The Journal of nutrition. 2017;147(6):1174-82.
17. Siervo M, Lara J, Chowdhury S, Ashor A, Oggioni C, Mathers JC. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. British Journal of Nutrition. 2015;113(1):1-15.
18. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA: a cancer journal for clinicians. 2012;62(1):30-67.

19. Clinton SK, Giovannucci EL, Hursting SD. The World Cancer Research Fund/American Institute for Cancer Research Third Expert Report on Diet, Nutrition, Physical Activity, and Cancer: Impact and Future Directions. The Journal of nutrition. 2019.
20. Sharif Y, Sadeghi O, Benisi-Kohansal S, Azadbakht L, Esmaillzadeh A. Legume and Nuts Consumption in Relation to Odds of Breast Cancer: A Case-Control Study. Nutrition and Cancer. 2020:1-10.
21. Hammad SS, Mahmoud R, Marie L, Abdelrahim D, Tayyem RF. Association between grain and legume intakes and breast cancer risk among women. Annals of Cancer Research and Therapy. 2020;28(2):81-7.
22. Kazemi A, Barati-Boldaji R, Soltani S, Mohammadipoor N, Esmaeilinezhad Z, Clark CC, et al. Intake of various food groups and risk of breast cancer: A systematic review and dose-response meta-analysis of prospective studies. Advances in Nutrition. 2021;12(3):809-49.
23. Peng C, Luo W-P, Zhang C-X. Fruit and vegetable intake and breast cancer prognosis: a meta-analysis of prospective cohort studies. British Journal of Nutrition. 2017;117(5):737-49.
24. Jones-McLean E, Hu J, Greene-Finestone L, de Groh M. A DASH dietary pattern and the risk of colorectal cancer in Canadian adults. Health promotion and chronic disease prevention in Canada: research, policy and practice. 2015;35(1):12.
25. Miller PE, Cross AJ, Subar AF, Krebs-Smith SM, Park Y, Powell-Wiley T, et al. Comparison of 4 established DASH diet indexes: examining associations of index scores and colorectal cancer–. The American journal of clinical nutrition. 2013;98(3):794-803.
26. Ali Mohsenpour M, Fallah-Moshkani R, Ghiasvand R, Khosravi-Boroujeni H, Mehdi Ahmadi S, Brauer P, et al. Adherence to Dietary Approaches to Stop Hypertension (DASH)-style diet and the risk of cancer: A systematic review and meta-analysis of cohort studies. Journal of the American College of Nutrition. 2019;38(6):513-25.
27. Abdollahi M, MOHAMMADI NF, Houshiarrad A, GHAFARPOUR M, Ghodsi D, Kalantari N. Socio-economic differences in dietary intakes: the comprehensive study on household food consumption patterns and nutritional status of IR Iran. 2014.
28. Hashemi SZ, Vahidinia A, Hazavehei SMM, Karimi-Shahanjarini A, Poorolajal J, Erfani H, et al. Low compliance with dietary recommendations among Iranian women: a dietary pattern survey. Progress in Nutrition. 2019;21:234-43.
29. Naja F, Nasreddine L, Awada S, El Sayed Ahmad R, Hwalla N. Nutrition in the prevention of breast cancer: a Middle Eastern perspective. Frontiers in public health. 2019;7:316.
30. Jessri M, Mirmiran P, Golzarand M, Rashidkhani B, Hosseini-Esfahani F, Azizi F. Comparison of trends in dietary pattern in Iran, Middle Eastern and North African countries from 1961 to 2005. Pajoohandeh Journal. 2011;16(1):1-10.
31. Mehio Sibai A, Nasreddine L, Mokdad AH, Adra N, Tabet M, Hwalla N. Nutrition Transition and Cardiovascular Disease Risk Factors in Middle East and North Africa Countries: Reviewing the Evidence. Annals of Nutrition and Metabolism. 2010;57(3-4):193-203.
32. Hwalla N, Weaver CM, Mekary RA, El Labban S. public health nutrition in the Middle East. Frontiers in public health. 2016;4:33.
33. Di Castelnuovo A, Costanzo S, Bagnardi V, Donati MB, Iacoviello L, De Gaetano G. Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. Archives of internal medicine. 2006;166(22):2437-45.
34. Amin-Esmaeili M, Rahimi-Movaghar A, Sharifi V, Hajebi A, Mojtabai R, Radgoodarzi R, et al. Alcohol use disorders in Iran: Prevalence, symptoms, correlates, and comorbidity. Drug and alcohol dependence. 2017;176:48-54.
35. Esfahani FH, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. Journal of epidemiology. 2010;20(2):150-8.
36. Sasanfar B, Toorang F, Esmaillzadeh A, Zendehdel K. Adherence to the low carbohydrate diet and the risk of breast Cancer in Iran. Nutrition Journal. 2019;18(1):86.

37. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Archives of internal medicine. 2008;168(7):713-20.
38. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. The American journal of clinical nutrition. 1997;65(4):1220S-8S.
39. Armstrong T, Bull F. Development of the world health organization global physical activity questionnaire (GPAQ). Journal of Public Health. 2006;14(2):66-70.
40. Petimar J, Park Y-MM, Smith-Warner SA, Fung TT, Sandler DP. Dietary index scores and invasive breast cancer risk among women with a family history of breast cancer. The American journal of clinical nutrition. 2019;109(5):1393-401.
41. Haridass V, Ziogas A, Neuhausen SL, Anton-Culver H, Odegaard AO. Diet quality scores inversely associated with postmenopausal breast cancer risk are not associated with premenopausal breast cancer risk in the California teachers study. The Journal of nutrition. 2018;148(11):1830-7.
42. Kaaks R, Lukanova A. Energy balance and cancer: the role of insulin and insulin-like growth factor-I. Proceedings of the nutrition society. 2001;60(1):91-106.
43. Gupta K, Krishnaswamy G, Karnad A, Peiris AN. Insulin: a novel factor in carcinogenesis. The American journal of the medical sciences. 2002;323(3):140-5.
44. Cho E, Chen WY, Hunter DJ, Stampfer MJ, Colditz GA, Hankinson SE, et al. Red meat intake and risk of breast cancer among premenopausal women. Archives of internal medicine. 2006;166(20):2253-9.
45. Guo J, Wei W, Zhan L. Red and processed meat intake and risk of breast cancer: a meta-analysis of prospective studies. Breast cancer research and treatment. 2015;151(1):191-8.
46. Aune D, Chan D, Vieira A, Rosenblatt DN, Vieira R, Greenwood D, et al. Fruits, vegetables and breast cancer risk: a systematic review and meta-analysis of prospective studies. Breast cancer research and treatment. 2012;134(2):479-93.
47. McGuire S. World cancer report 2014. Geneva, Switzerland: World Health Organization, international agency for research on cancer, WHO Press, 2015. Oxford University Press; 2016.
48. Lopes HF, Walle T, Nashar K, Egan BM. P-246: Total antioxidant capacity, an important factor affecting blood pressure responses to diet? American Journal of Hypertension. 2002;15(S3):119A.
49. Tayyem RF, Mahmoud RI, Shareef MH, Marei LS. Nutrient intake patterns and breast cancer risk among Jordanian women: a case-control study. Epidemiology and health. 2019;41.
50. Heath AK, Muller DC, van den Brandt PA, Papadimitriou N, Critselis E, Gunter M, et al. Nutrient-wide association study of 92 foods and nutrients and breast cancer risk. Breast Cancer Research. 2020;22(1):1-12.
51. Assi N, Moskal A, Slimani N, Viallon V, Chajes V, Freisling H, et al. A treelet transform analysis to relate nutrient patterns to the risk of hormonal receptor-defined breast cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). Public health nutrition. 2016;19(2):242-54.
52. Fereidani SS, Eini-Zinab H, Heidari Z, Jalali S, Sedaghat F, Rashidkhani B. Nutrient patterns and risk of breast cancer among Iranian women: a case-control study. Asian Pacific journal of cancer prevention: APJCP. 2018;19(9):2619.
53. Most MM. Estimated phytochemical content of the dietary approaches to stop hypertension (DASH) diet is higher than in the Control Study Diet. Journal of the American Dietetic Association. 2004;104(11):1725-7.
54. Chavez-Santoscoy R, Gutierrez-Uribe J, Serna-Saldívar S. Phenolic composition, antioxidant capacity and in vitro cancer cell cytotoxicity of nine prickly pear (Opuntia spp.) juices. Plant Foods for Human Nutrition. 2009;64(2):146-52.
55. Ray G, Batra S, Shukla NK, Deo S, Raina V, Ashok S, et al. Lipid peroxidation, free radical production and antioxidant status in breast cancer. Breast cancer research and treatment. 2000;59(2):163-70.

56. Sasanfar B, Toorang F, Maleki F, Esmaillzadeh A, Zendehdel K. Association between dietary total antioxidant capacity and breast cancer: a case–control study in a Middle Eastern country. Public Health Nutrition. 2020:1-8.
57. Hodson L, Harnden K, Roberts R, Dennis A, Frayn K. Does the DASH diet lower blood pressure by altering peripheral vascular function? Journal of human hypertension. 2010;24(5):312-9.
58. Azadbakht L, Surkan PJ, Esmaillzadeh A, Willett WC. The Dietary Approaches to Stop Hypertension eating plan affects C-reactive protein, coagulation abnormalities, and hepatic function tests among type 2 diabetic patients. The Journal of nutrition. 2011;141(6):1083-8.
59. Onvani S, Haghighatdoost F, Azadbakht L. Dietary approach to stop hypertension (DASH): diet components may be related to lower prevalence of different kinds of cancer: A review on the related documents. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2015;20(7):707.
60. Esfandiari S, Bahadoran Z, Mirmiran P, Tohidi M, Azizi F. Adherence to the dietary approaches to stop hypertension trial (DASH) diet is inversely associated with incidence of insulin resistance in adults: the Tehran lipid and glucose study. Journal of clinical biochemistry and nutrition. 2017:16-95.
61. Corsino L, Sotres-Alvarez D, Butera NM, Siega-Riz AM, Palacios C, Pérez CM, et al. Association of the DASH dietary pattern with insulin resistance and diabetes in US Hispanic/Latino adults: results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). BMJ Open Diabetes Research and Care. 2017;5(1):e000402.
62. Schairer C, Gadalla SM, Pfeiffer RM, Moore SC, Engels EA. Diabetes, abnormal glucose, dyslipidemia, hypertension, and risk of inflammatory and other breast cancer. Cancer Epidemiology and Prevention Biomarkers. 2017;26(6):862-8.
63. Martin SD, McGee SL. Metabolic reprogramming in type 2 diabetes and the development of breast cancer. Journal of Endocrinology. 2018;237(2):R35-R46.
64. Goldin BR, Woods MN, Spiegelman DL, Longcope C, Morrill-LaBrode A, Dwyer JT, et al. The effect of dietary fat and fiber on serum estrogen concentrations in premenopausal women under controlled dietary conditions. Cancer. 1994;74(S3):1125-31.
65. Aubertin-Leheudre M, Gorbach S, Woods M, Dwyer JT, Goldin B, Adlercreutz H. Fat/fiber intakes and sex hormones in healthy premenopausal women in USA. The Journal of steroid biochemistry and molecular biology. 2008;112(1-3):32-9.
66. Dong J-Y, Zhang L, He K, Qin L-Q. Dairy consumption and risk of breast cancer: a meta-analysis of prospective cohort studies. Breast cancer research and treatment. 2011;127(1):23-31.
67. Zhang C-X, Ho SC, Fu J-H, Cheng S-Z, Chen Y-M, Lin F-Y. Dairy products, calcium intake, and breast cancer risk: a case-control study in China. Nutrition and cancer. 2011;63(1):12-20.
68. Carroll KK, Jacobson EA, Eckel LA, Newmark HL. Calcium and carcinogenesis of the mammary gland. The American journal of clinical nutrition. 1991;54(1):206S-8S.
69. Aro A, Männistö S, Salminen I, Ovaskainen M-L, Kataja V, Uusitupa M. Inverse association between dietary and serum conjugated linoleic acid and risk of breast cancer in postmenopausal women. Nutrition and cancer. 2000;38(2):151-7.
70. Shultz T, Chew B, Seaman W. Differential stimulatory and inhibitory responses of human MCF-7 breast cancer cells to linoleic acid and conjugated linoleic acid in culture. Anticancer research. 1992;12(6B):2143-5.
71. Willett W. Nutritional epidemiology: Oxford University Press; 2012.