

Healthy dietary patterns and the risk of breast cancer: A review of current data

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Abstract: There is growing evidence that healthy dietary patterns including Mediterranean, prudent, traditional and plant-food based dietary patterns could have favorable effects in breast cancer prevention but there are inconsistencies in this regard. In the current study we reviewed the current evidences in relation to healthy dietary patterns and the risk of breast cancer. Both positive and negative association between Mediterranean dietary pattern and scores as well as prudent and traditional diet and breast cancer risk were observed in case-control and cohort studies. These conflicting findings might be explained by several issue including different dietary assessment methods, different definitions of Mediterranean dietary pattern and score, measurement errors, race differences, and potential confounding variables adjusted in the models. The healthy dietary patterns with high loading of fruits, vegetables, whole grains and legumes had been mainly accompanied with a considerable reduced risk of breast cancer in different races. It should be noted that menopausal and tumor's hormone receptor status, as well as body mass index of women had determinant role in the association of healthy dietary patterns and breast cancer risk. Protective effects of healthy dietary patterns against breast cancer were mainly observed in women with normal body weight (BMI<25 kg/m²). Further studies are required to clear the associations of dietary patterns and breast cancer risk.

Keywords: Breast Cancer, Dietary Pattern, Mediterranean Diet, Prudent/Healthy Dietary Pattern, Traditional Diet

1. Introduction

Breast cancer is the most common diagnosed cancer in female and the leading cause of cancer mortality in women around the world (1). Various factors including genetic background, familial history of breast cancer, race and ethnicity, pregnancy and breast feeding status, menstrual history, hormone replacement therapy, smoking, alcohol consumption, relative body weight, lifestyle and environmental factors have been proposed as main contributors for breast cancer incidence (2, 3). Dietary patterns and food components are considered as main modifiable risk factors for development of breast cancer (4, 5). Several studies showed that dietary intake of macro and micronutrients as well as various food groups including fruits and vegetables, phytochemical-rich foods, dairy and meat products may be related to the risk of breast cancer (6-8); moreover it has been investigated that dietary patterns beyond the dietary components have effective role on breast

cancer incident (9-11). Protective effects of some dietary patterns such as prudent/healthy pattern, plant-based and Mediterranean diet rich in fruits and vegetables, whole grains, nuts and fish meat against the development of breast cancer has been reported; on the other hand, some epidemiological studies showed that western/unhealthy patterns generally characterized by high amount of refined carbohydrate, processed meats and fast foods increased the risk of breast cancer in both premenopausal and postmenopausal women (12-14). However, some investigations showed no significant association between dietary patterns and breast cancer risk (15, 16). Our aim here is to comprehensively review the current evidences in relation to healthy dietary patterns and the risk of breast cancer. We obtained relevant articles, including case-control, cross-sectional and cohort studies with appropriate design, as well as review articles with good quality, published between 1990 to 2014, through searches of the Medline and PubMed databases.

2. Mediterranean Dietary Pattern and Risk of Breast Cancer

Mediterranean diet generally characterized as a diet rich in fruits and vegetables, legumes, nuts, whole grains, mono-unsaturated fats and fish meat, relatively poor in dairy and meat products, and poor in saturated fats; Mediterranean dietary pattern may also defined by the four dietary indicators including high monounsaturated to saturated fatty acid ratio (1.6-2.0), high dietary fiber (41-62 g/day), high dietary antioxidant capacity (3500-5300 trolox equivalent/day) and high phytosterols (370-555 mg/day) (17). Adherence to Mediterranean diet has been investigated as a protective factor against some non-communicable chronic diseases including cardiovascular disease, diabetes and many type of cancer (18). Although some studies showed that Mediterranean diet decrease the risk of breast cancer, the association of Mediterranean dietary pattern and the incidence of breast cancer is controversial.

In Swedish Women's Lifestyle and Health cohort study included 49,258 women aged 30 to 49 years, adherence to Mediterranean dietary pattern was not significantly associated with the risk of breast cancer; relative risk for breast cancer per a two point increase in Mediterranean diet score was 1.08 (95% confidence interval: 1.00–1.15) in all women, and 1.10 (95% CI: 1.01-1.21) and 1.02 (95% CI: 0.91–1.15) in premenopausal and postmenopausal women, respectively (15). A 9-year follow-up of women participated in the UK Women's Cohort Study reported no statistically significant association between Mediterranean dietary pattern and the risk of breast cancer in overall; in premenopausal women, maximal compared with minimal adherence to Mediterranean diet was associated with decreased the risk of breast cancer by 35% (hazards ratio: 0.65, 95% CI: 0.42-1.02, P for trend=0.09), but in postmenopausal women, no significant trend were observed (19). In a 10-year follow-up period among 65,374 women from the E3N-EPIC cohort study, healthy/Mediterranean pattern, characterized by higher consumption of vegetables, fruits, seafood, olive and sunflower oil, was negatively associated with breast cancer risk (HR: 0.85, 95% CI: 0.75-0.95; P for linear trend=0.003), especially in women with estrogen receptor-positive/progesterone receptor-negative tumors (20).

In another prospective cohort, the relative risk for estrogen negative (ER-) breast cancer tumor was 0.79 (95% CI: 0.60-1.03, P for trend=0.03) in the highest compared to the lowest quintile category of Mediterranean diet score; estrogen positive (ER+) breast cancer tumor was also not statistically related to Mediterranean diet score (21). A 8-year follow-up of 335,062 pre- and postmenopausal women in the European prospective investigation into cancer and nutrition cohort (EPIC) study showed that Mediterranean diet score was inversely associated with the risk of BC overall and in postmenopausal women (HR: 0.94, 95% CI: 0.88-1.00; P for trend= 0.048, and HR: 0.93, 95% CI: 0.87-0.99; P for trend= 0.037, in high vs. low score, respectively) but not in premenopausal women; The association was more

pronounced in ER- or PR- tumors (HR: 0.80, 95% CI: 0.65-0.99; P for trend= 0.043) (22).

In the Greek EPIC cohort, increasing adherence to the Mediterranean diet was not associated with lower breast cancer risk in the overall (HR: 0.88, 95% CI: 0.75-1.03, for each 2 point] or in premenopausal women (HR: 1.01, 95% CI: 0.80-1.28), but a marginally significant inverse association was observed among postmenopausal women (HR: 0.78, 95% CI: 0.62-0.98) (23).

A case-control study reported no significant association between Mediterranean diet score and breast cancer risk in Greek-Cypriot women, however, higher intake of vegetables and salads (OR per unit increase in servings/week: 0.95, 95% CI: 0.92-0.99), fish (OR per unit increase in servings/week: 0.88, 95% CI: 0.79-0.98), and olive oil (OR per unit increase in servings/week: 0.95, 95% CI: 0.92-0.99) was associated with a significant reduced risk of breast cancer; moreover a dietary pattern similar to Mediterranean pattern were derived using principal component analysis, included vegetables, fruit, fish and legumes, was related to reduced risk of breast cancer (OR: 0.67, 95% CI: 0.49-0.92 highest compared to the lowest quartile, P for trend < 0.0001) (24). Consistent with these results, another population-based case-control study among Asian-American women, showed a significant inverse association between conformity to the Mediterranean dietary pattern and the risk of breast cancer (OR: 0.65, 95% CI: 0.44-0.95, highest compared to lowest score) (25). Mediterranean dietary patterns were also associated with lower risk of breast cancer (OR: 0.76, 95% CI: 0.63-0.92, highest compared to lowest quartile, respectively; P for trend< 0.01) in a case-control study in among Hispanic women than among non-Hispanic white women (26).

In general, both protective and null effect of Mediterranean dietary pattern in relation to breast cancer risk were observed in case-control and cohort studies; These conflicting findings might be explained by several issue including different dietary assessment methods, different definitions of Mediterranean dietary pattern and score, measurement errors, race differences, and potential confounding variables adjusted in the models.

Despite the inconsistency in the association of Mediterranean and breast cancer risk, several plausible mechanisms have been proposed to describe some observed protective effect of the Mediterranean diet against breast cancer risk. First of these is the modulatory effect of Mediterranean diet on metabolism of estrogen; the results of a clinical trial showed that adherence to Mediterranean diet reduced endogenous estrogen levels and total urinary estrogens and their metabolites related to development of breast cancer (including classical estrogens and especially hydroxy-derivatives) (27). The second anti-cancer aspect of Mediterranean diet has been attributed to high phytochemical content; dietary carotenoids such as β -carotene, lutein, zeaxanthin, as well as polyphenols have preventive effects against incidence of breast cancer (28-30). Studies showed that these phytochemicals could inhibit phase I enzymes, induction of phase II enzymes, scavenge DNA reactive

agents, suppress the abnormal proliferation of early and pre-neoplastic lesions, and inhibit certain properties of the cancer cell (31). Phytochemicals could also regulate steroid hormone and estrogen metabolism, inhibit cell adhesion and invasion, induce expression of tumor suppressor genes, cell cycle arrest and apoptosis, and modulate various important signal transduction pathways (32). Lipid composition of Mediterranean diet (higher levels of mono-unsaturated fatty acids and lower levels of saturated and industrial-trans fatty acids) is another possible mechanism may describe protective effects of this diet against breast cancer (33,34).

3. Prudent/Healthy and Traditional Dietary Patterns and Risk of Breast Cancer

The Prudent dietary pattern is generally characterized by high intakes of vegetables, fruits, whole grain products and low intakes of refined grain products. Brenna et al. in a meta-analysis of cohort and case-control studies reported an evidence showed that the risk of breast cancer in the highest compared to the lowest categories of prudent/healthy pattern reduced (OR: 0.89, 95% CI: 0.82-0.99, *P* for trend=0.02); in this meta-analysis prudent/healthy pattern had high-factor loading for plant foods and low-factor loading for red and processed meat products (35). One cohort analysis on the Nurses Health Study II showed that there was no significant association between prudent dietary pattern and risk of breast cancer after 8-years of follow-up (OR: 0.90, 95% CI: 0.68-1.18, *P* for trend = 0.54) (36).

Prudent pattern which had greatest loading on fruit and non-starchy vegetables, in a cross-sectional study showed a protective effect against breast cancer (OR: 0.56, 95 % CI: 0.41–0.77, highest compared to the lowest tertile) (37). Surprisingly in another study, prudent pattern with high loading for low-fat dairy, whole grains, fruit and fruit juice, legumes, vegetables, and soups was associated with higher risk of breast cancer (OR: 1.42, 95% CI: 1.14-1.77; *P* for trend= 0.01) (26).

A cohort analysis conducted in the Black Women's Health Study revealed that prudent diet had weakly association with breast cancer risk in overall, but a reduced risk of breast cancer was observed in women with a BMI< 25 and highest conformance to prudent dietary pattern (incident rate ratio: 0.64, 95% CI: 0.43, 0.93; *P* for trend= 0.01); in this study prudent dietary pattern was also associated with a lower risk of breast cancer in premenopausal women (IRR: 0.70; 95% CI: 0.52, 0.96; *P* for trend= 0.01), and we found a significant inverse association for the prudent dietary pattern and estrogen receptor–negative breast cancer (incident rate ratio: 0.52, 95% CI: 0.28-0.94; *P* for trend= 0.01) (38).

There is evidence that some traditional diets have protective properties against breast cancer while in some population, traditional dietary pattern were positively associated with breast cancer; this diversity is mainly attributed to the food components of traditional patterns

among different population. Conformance of a traditional southern US traditional diet characterized by cooked greens and legumes, low-mayonnaise-salad, sweet potatoes, and cabbage, non-significantly reduced postmenopausal breast cancer risk in overall, and significantly reduced invasive breast cancer risk (relative hazard: 0.78, 95% CI: 0.65-0.95, *P* for trend= 0.003). This diet was also associated with reduced risk in women who had no familial history of breast cancer or who had BMI<25 (39). In contrast, a case-control study in Argentina showed that traditional dietary pattern, defined as fat meats, bakery products, vegetable oil and mayonnaise, increased the risk of breast cancer (OR: 3.13, 95 % CI: 2.58–3.78, highest compared to the lowest tertile) (37). In a case-control investigation conducted in Four-Corners Breast Cancer Study, a Native Hispanic traditional diet, with higher loadings for Mexican cheeses, soups, meat dishes, legumes, and tomato-based sauces, showed a protective effect against breast cancer risk (*P*: 0.68, 95% CI: 0.55-0.85; *P* for trend< 0.01) (26).

In Japanese women, highest compared to the lowest quartile of prudent dietary pattern characterized by higher loading of vegetables, fruits, and fish was accompanied with 27% decreased risk of breast cancer (OR: 0.73, 95% CI: 0.63–0.84) (40).

4. Other Healthy Dietary Patterns and Risk of Breast Cancer

A prospective cohort among Italian women, after 9.5-years of follow-up showed that salad-vegetables dietary pattern rich in raw vegetables and olive oil was associated with the reduced risk of breast cancer (RR: 0.66, 95% CI: 0.47-0.95, in the highest compared to the lowest tertile; *P* for trend= 0.016); more interestingly women with body mass index <25 had a greater reduced risk in the highest tertile of salad vegetables pattern (RR: 0.39, 95% CI: 0.22-0.69; *P* for trend= 0.001), whereas protective effect of salad vegetables pattern was not observed in women with BMI ≥ 25 (41). In a 5-year follow-up among postmenopausal Singapore Chinese women, greater intake of the vegetable-fruit-soy dietary pattern characterized by cruciferous vegetables, fruit, and tofu products, was dose-dependently accompanied with decreasing trend in breast cancer risk (HR: 0.70, 95% CI: 0.51, 0.95, highest compared to lowest quartile; *P* for trend< 0.01) (42). A vegetable-fish/poultry-fruit dietary pattern, defined by principal components factor analysis in a large cohort of American women, had no significant association with breast cancer incidence (39). In a case-control study, women with the highest compared to the lowest conformance to a healthy dietary pattern rich in vegetable, fruit, soy, milk, poultry and fish had a 74% decreased risk of breast cancer (OR: 0.26, 95% CI: 0.17–0.42) (43). Similarly a case-control study among Uruguay women showed that healthy dietary pattern characterized by high loading of raw and cooked vegetables, total fruits, poultry, and fish was inversely related to breast cancer risk (OR: 0.46, 95% CI: 0.31–0.69) (44).

Another study in Uruguay women also revealed that antioxidant dietary pattern with higher loading on glucose, fructose, vitamin C, vitamin E, carotenoids, flavonoids and phytosterols, was related to reduced risk of breast cancer (OR: 0.44, 95% CI: 0.27-0.74, highest compared to the lowest quartile; *P* for trend=0.001) (45). A case-control investigation among Iranian women showed that higher compliance to a healthy dietary pattern characterized by high loading of vegetables, fruits, low-fat dairy products, legumes, olive and vegetable oils, fish, organ meat, poultry, pickles, soya and whole grains, was related to a considerable reduced risk of breast cancer (OR: 0.25, 95% CI: 0.08-0.78) (9).

5. Conclusion

Despite current inconsistent findings regarding the association of some healthy dietary patterns especially Mediterranean diet, prudent and traditional pattern with breast cancer risk, it is investigated that a healthy diet based on plant-foods including whole grains, legumes, vegetables and fruits as main sources of dietary fiber, phytochemicals and antioxidants could contribute to prevent the development of breast cancer and malignancies. It should be noted that the association of healthy dietary patterns and breast cancer risk may affect by menopausal and tumor's hormone receptor status including ER-/+ or PR-/+ , as well as body mass index of women. Protective effects of healthy dietary patterns against breast cancer were mainly observed in women with normal body weight (BMI<25 kg/m²). Further studies are required to clarify the associations of dietary patterns and breast cancer risk.

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