

Comparing an Olive Oil-Enriched Diet to a Standard Lower-Fat Diet for Weight Loss in Breast Cancer Survivors: A Pilot Study

Mary M. Flynn, Ph.D., R.D., L.D.N.,¹ and Steven E. Reinert, M.S.²

Abstract

Background: Traditional diets that include moderate to high intakes of extra virgin olive oil have been related to a decrease in breast cancer risk. We hypothesized that an olive oil-enriched diet would lead to greater weight loss and acceptance, compared with a standard diet, in women previously diagnosed with invasive breast cancer.

Methods: Participants consumed a National Cancer Institute (NCI) diet (total fat >15% and <30%) and a plant-based olive oil diet (PBOO; ≥ 3 tablespoons of olive oil/day) for 8 weeks, each with random assignment to the order. We established a weight loss goal of at least 5% of baseline weight. After completion of the two diet trials, each participant self-selected one of the diets for an additional 6 months of follow-up for weight management. Body measures were done before and after each diet and after follow-up; fasting blood samples were collected after each diet and after follow-up.

Results: Forty-four overweight women started and 28 completed the 44-week protocol. Twelve (80%) of the 15 women who started with the PBOO diet achieved a weight loss of $\geq 5\%$ compared to 4 (31%) of the 13 who started with the NCI diet ($p < 0.01$). Nineteen of the 22 women eligible for follow-up chose the PBOO diet, and all completed the study. Of the 3 women who chose the NCI diet for follow-up, 1 completed the study. The PBOO diet resulted in lower triglycerides (NCI 105 ± 46 mg/dL, PBOO 96 ± 37 mg/dL, $p = 0.06$) and higher high-density lipoprotein cholesterol (HDL-C) (NCI 64 ± 13 mg/dL, PBOO 68 ± 12 mg/dL, $p = 0.001$).

Conclusions: An olive oil-enriched diet brought about greater weight loss than a lower-fat diet in an 8-week comparison. Moreover, these women chose, overwhelmingly, the olive oil-enriched diet for 6 months of follow-up. An olive oil-enriched diet may be more efficacious for weight loss in breast cancer survivors than a standard lower-fat diet.

Introduction

OVERWEIGHT WOMEN WITH BREAST CANCER are at increased risk of disease recurrence and death.¹ Further, weight gain during breast cancer treatment is common and is related to poor prognosis.² The National Cancer Institute (NCI) lists obesity as a risk factor for disease recurrence³ but does not recommend a diet for weight loss, although it has consistently recommended lowering dietary fat to prevent breast cancer. Lower-fat diets have not been shown to decrease breast cancer risk,⁴ however, and also may not reduce breast cancer recurrence⁵ unless they result in weight loss.⁶ Diets more moderate in fat are associated with enhanced long-term weight management^{7,8} and healthier

levels of high-density lipoprotein cholesterol (HDL-C), triglycerides (TG),⁹ and insulin,¹⁰ all biomarkers for breast cancer (HDL and TG,¹¹ insulin¹²). Extra virgin olive oil has been associated with decreasing breast cancer risk in Greece, Spain, and Italy, with a dose-response trend,¹³ making it a potentially healthy dietary component for women with breast cancer.

There is a need to determine a food pattern that will lead to healthy weight management in women who have had breast cancer. This study compares a conventional lower-fat diet recommended for women diagnosed with breast cancer³ with a plant-based olive oil (PBOO) diet for weight loss, improvement in selected breast cancer biomarkers, and acceptance.

¹The Miriam Hospital and Brown University, Providence, Rhode Island.

²Lifespan Information Services, Providence, Rhode Island.

Subjects and Methods

Study subjects

Participants were overweight women diagnosed with invasive breast cancer after the age of 50 and within 4 years of completing treatment. Inclusion criteria were (1) body mass index (BMI) of 25.0–35.0 kg/m² or (2) weight gain of at least 10 kg from age 18 for women with a BMI <25.0 kg/m² (this weight gain has been related to increasing risk of postmenopausal breast cancer by 13%–18%¹⁴). Exclusion criteria were smokers, history of heart or kidney disease, and diabetes. Any medication had to be consumed as a stable dose for at least 4 weeks before starting the protocol, with no change during the study. Participants were recruited by fliers that were placed in physician offices and oncology treatment centers and newspaper advertisements. The principal investigator (PI) presented the study to several oncology physician groups. Recruitment was from September 2004 to November 2007.

Participants consumed two diets for 8 weeks of weight loss, each with random assignment of diet order: (1) an NCI diet for women with breast cancer³ and (2) PBOO diet. The PBOO diet was designed by the study PI and previously had been compared with lower-fat diets in patients with heart disease¹⁵ and in overweight but otherwise healthy participants.¹⁶ Both diets were prescribed at 1500 calories. The NCI diet had dietary fat of 25–50 g/day (>15% and <30% fat for 1500 calories); unlimited fruits and vegetables, with a minimum of 5 servings of fruits and vegetables/day; and up to 7 oz of lean meat/day. Canola oil was provided to the participants while on the NCI diet, as it is low in omega-6 polyunsaturated fats, which have been associated with an increase in breast cancer risk.^{17,18} The PBOO diet prescribed was for at least 3 tablespoons/day of extra virgin olive oil, with sufficient extra virgin olive oil provided during the PBOO diet; unlimited vegetables; 3 servings/day of fruit and up to 6 oz/week of poultry and up to 8 oz/week of seafood. Whole grain products and legumes were encouraged for both diets, and alcohol was proscribed.

Diet instruction was provided before each of the 8 weeks of weight loss. Participants were provided with meal plans, recipes, and instructions for following each of the diets. For the PBOO diet, the recipes were primarily vegetarian and included 1–2 tablespoons of extra virgin olive oil used to cook the vegetables. Participants were given a minimum weight loss goal of 5% from baseline weight. Participants met weekly with the PI or the study assistant.

After completing both diets, participants were asked to select one of the diets for 6 months of continued weight loss or weight management, with semimonthly meetings with research staff. Subjects were encouraged to maintain the diet of choice and to increase their physical activity. For the PBOO diet, they were instructed to use a minimum of 2 tablespoons of olive oil/day and were allowed up to 21 oz of poultry/seafood/week. Participants were not provided with either olive oil or canola oil during follow-up.

Three-day food diaries were kept during weeks 4 and 8 of each diet and during months 3 and 6 of the follow-up period. Data were analyzed using DietAnalysist+ V 8 (Thompson Wadsworth, 2007). Daily records of amount and type of dietary fat, fruit, vegetable, whole grains, and animal protein were recorded during the 8 weeks of weight loss and during 1 week/month in follow-up. Deviations from the diets were

assessed by the PI; participants unwilling to consume the diet as prescribed were removed from the study.

Measurements were done on days 1 and the day after each 8 weeks of diet were completed, which was the day of the final blood sample of each diet and at the end of the 6-month follow-up. These measurements were height by stadiometer, weight by balance beam, waist circumference at the smallest area of the torso, hips measured at the widest area of the buttocks, and bioelectric impedance analysis (BIA) (RJL, Inc Systems) for body composition. Weights were recorded weekly throughout the study. Two blood samples were taken at the end of each of the 8 weeks of weight loss, and one was taken after the 6 months of follow-up.

Laboratory analysis

Blood samples from each participant were run in the same analysis at Cardiovascular Research Associates, Inc., Boston, MA, as specified in the manufacturer's procedural documentation. Total cholesterol, TG, and HDL-C were measured by an enzymatic end point assay (Roche Diagnostics, Indianapolis, IN) on a Roche Diagnostics Hitachi 911 chemistry analyzer. High-sensitivity C-reactive protein (hsCRP) was measured by a turbidometric immunoassay (Wako Chemicals, Richmond, VA) on a Roche Diagnostics Hitachi 911 chemistry analyzer. Insulin was measured by a solid-phase, two-site chemiluminescent immunometric assay on an automated immunoassay system, IMMULITE[®] 1000, Diagnostic Product Corporation, Los Angeles, CA). Glucose was measured by a coupled enzymatic kinetic assay on an automated clinical chemistry analyzer (Olympus AU400, Olympus America Inc., Melville, NY), according to Stein.¹⁹ Carotenoids were extracted from plasma with hexane and analyzed by reversed-phase high-performance liquid chromatography (HPLC) using the method of Hess et al.²⁰ as modified by El-Sohemy et al.²¹ Carotenoids are detected at a wavelength of 300 nm.

Statistical analysis

This study was sized to provide 80% power in detecting a difference of 40% (80% vs. 40%) of women who achieved a weight loss of 5% on their respective diets. This calculation resulted in 28 subjects each of whom was assessed on both diets in the crossover trial design. We followed the crossover trial analysis approach of Pocock²²: (1) paired *t* tests comparing baseline to end point differences in outcomes between the two diet trials, (2) tests for a period effect, that is, if outcomes differ between the first administered vs. second administered trial, independent of diet type (independent samples *t* test), and (3) tests for interaction between treatment and period; that is, for each outcome, does the difference in treatment effect differ by period (independent samples *t* test)? For outcomes where significant period/interaction effects were found, we tested for a diet effect by comparing the patients who consumed the NCI diet first with the patients who consumed the PBOO diet first, using the independent samples *t* test.

We used the chi-square test to compare the percent of women who achieved a weight loss of ≥5% between the two diets (first-consumed diet only). We used an alpha probability of 0.05 as the threshold for statistical significance in two-tailed comparisons. Means are presented with standard deviations

(SD) throughout. All statistics were performed with Stata v. 8 (Stata Corp., College Station, TX).

The protocol was approved by the Internal Review Board of a Brown University Medical School teaching hospital. Participants signed informed consent.

Results

Forty-four women started the protocol, with 28 women completing the two 8-week periods of weight loss. Seven dropouts occurred during the NCI diet because of the subjects' inability to reduce their average dietary fat to <30%. Four of the 5 dropouts during the PBOO diet could not consistently include at least 3 tablespoons of olive oil daily; 1 woman dropped out during the PBOO diet because of an unwillingness to follow the protocol. Three women dropped out because of prescribed changes in their lipid-lowering medicines, and 1 had an unscheduled vacation.

Baseline characteristics of those completing both diets are presented in Table 1. Twenty-five of the 28 women qualified by BMI. The 3 women who qualified by weight gain from age 18 years had a mean BMI of 23.6 ± 1.1 kg/m² (mean gain 10.4 ± 0.45 kg, range 10.0–10.9 kg). Thirteen (46%) of the 28 women reported weight gain from diagnosis through cancer treatment (mean 6.7 ± 4.0 kg, range 1.4–15.9 kg). The average baseline BMI for the women who did not gain weight from diagnosis through cancer treatment was 27.8 ± 3.1 kg/m². Fifteen subjects received chemotherapy and 26 received radiation therapy as part of their treatment.

The change in anthropometrics and laboratory variables for each diet are presented in Table 2. The paired *t* test on percent change in body weight reveals a near significant trend for greater weight loss on PBOO; however, this analysis is skewed by a significant period effect (*p* < 0.001). Paired *t* tests performed separately for each period reveal that percent weight change was significantly greater for NCI vs. PBOO when NCI was consumed first (*n* = 13) (4.6 ± 1.5 NCI vs. 3.1 ± 1.7 PBOO, *p* = 0.001) and significantly greater for PBOO vs. NCI when PBOO was consumed first (*n* = 15) (3.3 ± 2.2 NCI vs. 6.5 ± 1.6 PBOO, *p* < 0.001). Because of the significant period effect, and a near significant treatment-period interaction effect (*p* = 0.10), we further analyzed percent weight change (and baseline variables) using only results from the first-administered diet for each subject. This showed that 12 of 15 women (80%) achieved a weight loss of ≥ 5% on the PBOO diet compared with 4 of 13 (31%) on the NCI diet (*p* < 0.01). Further, whereas no baseline measures differed between the two groups (Table 3), the 15 PBOO subjects exhibited signif-

TABLE 1. BASELINE CHARACTERISTICS OF 28 PARTICIPANTS COMPLETING TWO 8-WEEK PERIODS OF WEIGHT LOSS

Characteristic	Mean	Range
Age (years)	59.2 ± 6.1	52–73
BMI (kg/m ²)	27.9 ± 2.8	22.5–33.0
Percent body fat	41.6 ± 4.6	32.6–50.2
Percent fat-free mass	58.6 ± 5.1	49.8–72.4
Waist (cm)	87.1 ± 8.5	71.9–103.8
Hip (cm)	108.4 ± 6.4	97.4–123.5
Weight gain from age 18 years (kg)	17.3 ± 8.9	–2.3–37.0

TABLE 2. ANTHROPOMETRICS AND LABORATORY VARIABLES FOR 28 PARTICIPANTS COMPLETING TWO 8-WEEK PERIODS OF WEIGHT LOSS

Change	NCI	PBOO	<i>p</i>
Body weight (kg)	–2.7 ± 1.4	–3.6 ± 1.9	0.05 ^a
Body weight (%)	–3.9 ± 1.9	–4.9 ± 2.4	0.06 ^b
Waist (cm)	–2.6 ± 1.7	–3.4 ± 3.2	0.25
Hip (cm)	–1.8 ± 2.5	–2.9 ± 2.5	0.13
Body fat (%)	–1.4 ± 1.4	–1.9 ± 1.8	0.28
Fat-free mass (%)	+1.1 ± 1.7	+1.9 ± 1.8	0.12
Total cholesterol (mg/dL)	188 ± 19	191 ± 21	0.38
Triglycerides (mg/dL)	105 ± 46	96 ± 37	0.06
HDL-C (mg/dL)	64 ± 13	68 ± 12	0.001
LDL-C (mg/dL)	103 ± 18	103 ± 22	0.82
Glucose (mg/dL)	91 ± 8	91 ± 8	0.56
Insulin (μU/mL)	11 ± 4	10 ± 3	0.18
C-reactive protein (mg/L)	12.68 ± 1.5	10.99 ± 10.99	0.11
Total carotenoids (μg/dL)	137 ± 35	140 ± 36	0.67

^aComparisons by paired *t* test.

^bDiet order effect; see Results.

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NCI, National Cancer Institute diet; PBOO, plant-based olive oil diet.

icantly greater percent weight loss than the 13 NCI subjects (4.6 ± 1.5 NCI, 6.5 ± 1.6 PBOO, *p* < 0.01). There was no difference in change in fat-free mass, despite differences in reported intake of dietary protein (Table 3).

The diets followed in this report are shown in Table 4. During week 8 of the PBOO diet, 11 women reported eating ≥ 1500 kcal (range 1510–1855 kcal), and 2 reported eating < 1200 kcal. For the NCI diet, 18 women reported eating < 1200 kcal during week 8 (range 790–1160 kcal), and 2 reported eating ≥ 1500 kcal. The average weekly dietary fat intake during the NCI diet was 89.7 ± 44.8 g (range 11.8–225.0 g). The average weekly olive oil intake was 24.4 ± 3.5 tablespoons (range 19.8–38.6).

Of the 28 women who completed both weight loss diets, 22 were eligible for the follow-up study; funding for the grant that supported the study ended when the remaining 6 women

TABLE 3. COMPARISONS OF BASELINE VARIABLES (BY INDEPENDENT SAMPLES *t* TEST) BETWEEN 13 SUBJECTS WHO CONSUMED NCI DIET FIRST VERSUS 15 SUBJECTS WHO CONSUMED PBOO DIET FIRST

Baseline measure	NCI	PBOO	<i>p</i>
Age	58.0 (5.3)	59.7 (7.0)	0.49
BMI	27.1 (2.6)	28.6 (2.9)	0.18
Percent body fat	39.8 (6.0)	42.6 (4.7)	0.23
Percent fat-free mass	59.7 (5.7)	57.7 (4.4)	0.29
Height (cm)	162.4 (6.2)	161.9 (5.2)	0.82
Waist	85.1 (7.7)	89.2 (9.7)	0.27
Hip	107.2 (6.3)	109.9 (6.7)	0.29
Weight at 18 years (kg)	120.3 (12.0)	125.0 (19.5)	0.48
Weight gain from 18 years (kg)	16.7 (6.7)	17.8 (10.8)	0.75
Weight, fat	60.4 (13.6)	72.1 (15.4)	0.09

BMI, body mass index; NCI, National Cancer Institute diet; PBOO, plant-based olive oil diet.

TABLE 4. MEAN (STANDARD DEVIATION) REPORTED FOR EACH WEIGHT LOSS DIET (N=28)

Week 8 3-day diet diary	NCI	PBOO	p
Energy (kJ)	1142 ± 208	1466 ± 201	<0.001 ^a
Percent protein	22 ± 4	13 ± 2	<0.001 ^a
Percent carbohydrate	61 ± 7	46 ± 6	<0.001 ^a
Fiber (g)/1000 calories	19 ± 4	21 ± 5	0.08 ^a
Percent total fat	21 ± 6	47 ± 5	<0.001 ^a
Total grams of fat	27 ± 10	77 ± 11	<0.001 ^a
Weekly average intake from daily records			
Vegetable	21.6 ± 6.1	29.9 ± 5.4	<0.001 ^b
Fruit	16.9 ± 6.8	16.4 ± 5.6	0.65 ^b
Fruit and vegetables	38.6 ± 9.3	46.3 ± 7.7	<0.001 ^b
Whole grains	21.9 ± 6.1	22.8 ± 5.8	0.56 ^b

^aComparisons by paired *t* test.

^bComparisons by Wilcoxon signed rank test.

NCI, National Cancer Institute diet; PBOO, plant-based olive oil diet.

would have entered follow-up. Nineteen (86%) of the 22 women chose the PBOO diet for follow-up. Among the 3 selecting the NCI diet, 2 dropped out after 1 month of follow-up. Thus, of the 20 women who completed the entire protocol, 19 followed the PBOO diet as prescribed for the 6 months of follow-up (Table 5). Laboratory values after 6 months of the PBOO diet compared with the values after the second trial of weight loss are presented in Table 6. Total blood carotenoid levels were significantly increased after 6 months on the PBOO diet compared with the end of weight loss. The increase in total cholesterol after 6 months of the PBOO diet was primarily due to a further increase in HDL-C.

Discussion

These results provide evidence that a PBOO diet may be more efficacious for weight loss in breast cancer survivors than a standard lower-fat diet. Both the lower-fat diet recommended by the NCI and the PBOO diet produced weight loss, but significantly more women (80%) lost at least 5% of their baseline weight when their first 8 weeks of weight loss diet were on the PBOO diet than when their first diet was the NCI (31%). In addition, the PBOO diet was clearly favored by

the women as a diet they would use long term; more women chose it for the 6 months of follow-up, and all 19 who chose it completed the 6 months of follow-up and either maintained their weight loss or lost additional weight. Support for the greater acceptability of the PBOO diet compared with the NCI diet comes from anecdotal comments from the participants who offered that (1) the PBOO diet was substantially more palatable than the lower-fat NCI diet, (2) they were not hungry between meals on the PBOO diet, yet they were losing weight, (3) the PBOO diet was easier to prepare, and (4) the PBOO diet was very economical. A future study will include a tool to better measure these attributes.

The NCI lists high-calorie, high-fat diets as risk factors for recurrence of breast cancer,³ although not all studies conclude that dietary fat increases cancer risk.¹³ The Women's Health Initiative (WHI) study was designed to determine if a low-fat diet would reduce breast cancer risk, and the results were that it did not.⁴ Participants in the WHI study did not achieve the goal of a 20% fat diet, and the authors suggest that this may have affected the results. As diets with <20% dietary fat have been related to an increase in breast cancer risk,¹³ it may have been providential that the women were not able to eat lower-fat diets. Results from trials testing the effect of low-fat diets

TABLE 5. MEAN (STANDARD DEVIATION) DIET REPORTED FOR WEEK 8 OF PBOO VERSUS AFTER 6 MONTHS (N=19)

3-day diet diary	Week 8	6 months	p ^a
Energy (kJ)	1462 ± 203	1446 ± 244	0.80
Percent protein	13 ± 2	14 ± 3	0.89
Percent carbohydrate	47 ± 7	48 ± 5	0.70
Fiber (g)/1000 calories	20 ± 5	18 ± 4	0.20
Percent total fat	47 ± 5	42 ± 5	0.01
Weekly average intake from daily records			p ^b
Extra virgin olive oil (Tablespoons)	24.4 ± 3.5	20.9 ± 4.4	0.001
Fruit (servings)	16.4 ± 5.6	16.8 ± 8.5	0.76
Vegetables (servings)	29.9 ± 5.4	28.9 ± 6.8	0.29
Fruit and vegetable (servings)	46.3 ± 7.7	45.6 ± 11.7	0.72
Whole grains (servings)	22.8 ± 5.8	22.6 ± 7.6	0.92

p-values should be interpreted as an index to the strength of relationship only, as tests may be underpowered to form conclusions of statistical significance.

^aComparisons by paired *t* tests.

^bComparisons by Wilcoxon signed rank test.

TABLE 6. COMPARISONS OF VARIABLES FROM END OF SECOND DIET TO AFTER 6 MONTHS (N=19)

	End of weight loss	After 6 months	P ^a
Weight (kg)	67.97 ± 8.81	66.88 ± 8.72	0.07
Total cholesterol (mg/dL)	193 ± 22	202 ± 32	0.01
Triglycerides (mg/dL)	100 ± 31	90 ± 29	0.19
HDL-C (mg/dL)	65 ± 11	73 ± 13	<0.001
LDL-C (mg/dL)	108 ± 22	111 ± 27	0.31
Glucose (mg/dL)	91 ± 7.7	90 ± 7.0	0.87
Insulin (μU/mL)	10.4 ± 3.8	9.9 ± 3.4	0.40
C-reactive protein (mg/L)	1.46 ± 1.4	1.46 ± 1.4	0.99
Total carotenoids (μmol/L)	134 ± 29	150 ± 42	0.02

p-values should be interpreted as an index to the strength of relationship only, as tests may be underpowered to form conclusions of statistical significance.

^aComparisons by paired *t* tests.

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

on recurrence have been mixed. The Women's Intervention Nutrition Study (WINS) results indicated that a low-fat diet that leads to weight loss improves relapse-free survival.⁶ However, the Women's Healthy Eating and Living (WHEL) study, which also included a low-fat diet, did not reduce breast cancer recurrence or mortality.⁵ Other studies have concluded that low-fat diets are not easily followed long term.^{7,23}

The PBOO diet is a version of a Mediterranean diet, a traditional diet that has been associated with lower rates of breast cancer for more than 20 years.²⁴ Recent studies have indicated that a Mediterranean diet pattern in U.S. women is also related to a reduction in breast cancer risk.^{25,26} It is commonly thought that diets higher in fat are not healthy for women who have had breast cancer. In fact, this bias initially made recruitment for this study difficult. However, physician referral increased considerably during the last year of funding when women were consistently losing and maintaining their weight loss while on the PBOO diet.

The relationship of dietary fat to breast cancer and health is likely dependent on the food that is the source of fat and not the actual fat content. For example, meat, even lean red meat, is a source of fat, and frequent meat consumption has been related to an increased risk of breast cancer,²⁷⁻²⁹ yet the NCI does not recommend limiting meat. Meat consumption has also been related to an increased risk of obesity.^{30,31} The effect of polyunsaturated fats on breast cancer risk may depend on the type of fat. Both higher intake^{17,18} and breast tissue content³² of omega-6 fatty acids have been positively related to an increased risk of breast cancer, whereas the ratio of tissue content of omega-3/omega-6 has been inversely related to risk.³³ All polyunsaturated fatty acids are prone to oxidation,³⁴ however, and women with breast cancer have elevated oxidation compared with women without breast cancer.³⁵ Monounsaturated fats will not oxidize, theoretically making them a healthier choice for people with cancer. If the health benefits of olive oil were due to the monounsaturated fat content, olive oil and canola oil would be interchangeable. However, extra virgin olive oil has components beyond monounsaturated fat, not present in canola, that can decrease cancer risk. Extra virgin olive oil contains more alpha-tocopherol, the form of vitamin E that acts as an antioxidant, than other oils³⁶ and other phenolic antioxidants, including simple phenols (hydroxytyrosol, tyrosol), aldehydic secoir-

idoids, flavonoids, and lignans (acetoxypinoresinol, pinorenesinol).³⁷ Lignans have also been shown to favorably influence estrogen metabolism,³⁸ and high intakes of lignans have been related to decreasing breast cancer risk.³⁸⁻⁴⁰ In addition, extra virgin olive oil contains squalene,⁴¹ which has been shown to be a tumor inhibitor.⁴² It has been suggested that the squalene content of olive accounts in large part for the association of olive oil with diminished cancer risk.^{42,43} Olive oil is the only fat whose consumption has been related to decreasing breast cancer risk.¹³

Diets high in plant products are generally related to better health. Vegetarians have been shown to weigh less^{44,45} and have better health, with fewer chronic diseases, compared with omnivores.^{46,47} Many studies have shown the cancer protective properties of phytonutrients in a variety of plant products, although studies examining the relationship of vegetable and fruit consumption to breast cancer risk have had mixed results.⁴⁸ The lack of consistency in showing that plant products protect from breast cancer may be related to how the plant products were prepared before being consumed. For example, both intake of carotenoid-containing vegetables and fruits⁴⁹ and higher blood carotenoids⁵⁰ have been related to decreasing breast cancer risk. The NCI specifically recommends consuming "dark orange sources of produce to reduce the risk of cancer recurrence and death."³ However, carotenoids require dietary fat to be absorbed,⁵¹ and the NCI encourages lower-fat diets. Cooking in dietary fat maximizes carotenoid absorption,⁵² which may help explain some of the relationship of the Mediterranean diet to lower rates of cancer; people in countries following the Mediterranean diet typically eat vegetables cooked in olive oil. Although there was no difference in blood carotenoid levels after the two weight loss diets, the higher-fat PBOO diet increased blood carotenoids after 6 months, compared with the values at the beginning of the follow-up period. This suggests that sufficient time is needed to increase blood carotenoid levels. Clearly, carotenoid-rich foods should be consumed with dietary fat to reduce cancer risk. Diet recommendations for decreasing breast cancer risk and recurrence should include this information.

The women reported eating more total energy and dietary fat while on the PBOO diet, yet they lost more weight on the PBOO diet than on the NCI lower-fat diet. This was also observed in the pilot studies of the PBOO diet^{15,16} and in the

participants in the Dietary Intervention Randomized Control Trial (DIRECT).⁸ Weight loss diets that allow more food would be more appealing, as they should create less hunger. The women also reported eating less protein on the PBOO diet compared with the NCI diet, yet fat-free mass was not detrimentally affected.

As expected, the PBOO diet lowered triglycerides and raised HDL-C relative to the NCI diet. It was anticipated that the PBOO diet would result in lower insulin levels, as extra virgin olive oil has been shown to lower insulin,⁵³ but this did not occur. Possibly, the greater restriction of energy for some of the participants on the NCI diet obscured potential diet composition differences.

Conclusions

Weight loss can be achieved with a variety of diets. Ideally, weight loss diets should comprise primarily foods that improve health. The PBOO diet tested in this study was designed to contain primarily foods that the literature has found to improve health. The women in this study reported the PBOO to be appetizing, and the foods included were readily available and affordable. Future studies incorporating more participants and longer diet periods could further illuminate weight management and health benefits.

Acknowledgments

This study was supported by a grant from The Susan G. Komen for the Cure Foundation.

Disclosure Statement

The authors have no conflicts of interest to report.

References

- Kroenke CH, Chen WY, Rosner B, Holmes MD. Weight, weight gain, and survival after breast cancer diagnosis. *J Clin Oncol* 2005;23:1370–1378.
- Irwin ML, McTiernan A, Baumgartner RN, et al. Changes in body fat and weight after a breast cancer diagnosis: Influence of demographic, prognostic, and lifestyle factors. *J Clin Oncol* 2005;23:774–782.
- Nutrition in Cancer Care. Cancer prevention/breast cancer. Available at www.cancer.gov/cancertopics/pdq/prevention/breast/patient/. Accessed September 1, 2008.
- Prentice RL, Caan B, Chlebowski RT, et al. Low-fat dietary pattern and risk of invasive breast cancer: The Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA* 2006;295:629–642.
- Pierce JP, Natarajan L, Caan BJ, et al. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: The Women's Healthy Eating and Living (WHEL) randomized trial. *JAMA* 2007;298:289–298.
- Chlebowski RT, Blackburn GL, Thomson CA, et al. Dietary fat reduction and breast cancer outcome: Interim efficacy results from the Women's Intervention Nutrition Study. *J Natl Cancer Inst* 2006;98:1767–1776.
- McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low-fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord* 2001;25:1503–1511.
- Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 2008;359:229–241.
- Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: A meta-analysis of randomized controlled trials. *Arch Intern Med* 2006;166:285–293.
- Golay A, Allaz AF, Morel Y, de Tonnac N, Tankova S, Reaven G. Similar weight loss with low- or high-carbohydrate diets. *Am J Clin Nutr* 1996;63:174–178.
- Franky Dhaval S, Shilin Nandubhai S, Pankaj Manubhai S, Patel HR, Prabhudas Shankerbhai P. Significance of alterations in plasma lipid profile levels in breast cancer. *Integr Cancer Ther* 2008;7:33–41.
- Goodwin PJ, Ennis M, Pritchard KI, et al. Fasting insulin and outcome in early-stage breast cancer: Results of a prospective cohort study. *J Clin Oncol* 2002;20:42–51.
- Willett WC. Diet and breast cancer. *J Intern Med* 2001;249:395–411.
- Trentham-Dietz A, Newcomb PA, Egan KM, et al. Weight change and risk of postmenopausal breast cancer (United States). *Cancer Causes Control* 2000;11:533–542.
- Flynn MM. Comparison of a Mediterranean diet with an AHA diet for weight loss and metabolic improvement. National Cardiovascular Health Conference, 2002.
- Flynn MM. A Mediterranean diet may improve weight loss and weight loss maintenance. *FASEB J* 2002;16:a369.
- Sonestedt E, Ericson U, Gullberg B, Skog K, Olsson H, Wirfalt E. Do both heterocyclic amines and omega-6 polyunsaturated fatty acids contribute to the incidence of breast cancer in postmenopausal women of the Malmo diet and cancer cohort? *Int J Cancer* 2008;123:1637–1643.
- Wirfalt E, Mattisson I, Gullberg B, Johansson U, Olsson H, Berglund G. Postmenopausal breast cancer is associated with high intakes of omega6 fatty acids (Sweden). *Cancer Causes Control* 2002;13:883–893.
- Stein MW. Clinical methods of enzymatic analysis. Academic Press, 1965.
- Hess D, Keller HE, Oberlin B, Bonfanti R, Schuep W. Simultaneous determination of retinol, tocopherols, carotenes and lycopene in plasma by means of high-performance liquid chromatography on reversed phase. *Int J Vitam Nutr Res* 1991;61:232–238.
- El-Sohemy A, Baylin A, Kabagambe E, Ascherio A, Spiegelman D, Campos H. Individual carotenoid concentrations in adipose tissue and plasma as biomarkers of dietary intake. *Am J Clin Nutr* 2002;76:172–179.
- Pocock SJ. *Trials: A practical approach*. New York: John Wiley & Sons, 1983.
- Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: A randomized trial. *JAMA* 2005;293:43–53.
- Berrino F, Muti P. Mediterranean diet and cancer. *Eur J Clin Nutr* 1989;43 (Suppl 2):49–55.
- Fung TT, Hu FB, McCullough ML, Newby PK, Willett WC, Holmes MD. Diet quality is associated with the risk of estrogen receptor-negative breast cancer in postmenopausal women. *J Nutr* 2006;136:466–472.
- Murtaugh MA, Sweeney C, Giuliano AR, et al. Diet patterns and breast cancer risk in Hispanic and non-Hispanic white women: The Four-Corners Breast Cancer Study. *Am J Clin Nutr* 2008;87:978–984.

27. Dai Q, Shu XO, Jin F, Gao YT, Ruan ZX, Zheng W. Consumption of animal foods, cooking methods, and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2002;11:801–808.
28. Dos Santos Silva I, Mangtani P, McCormack V, Bhakta D, Sevak L, McMichael AJ. Lifelong vegetarianism and risk of breast cancer: A population-based case-control study among South Asian migrant women living in England. *Int J Cancer* 2002;99:238–244.
29. Gonzalez CA. The European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr* 2006;9:124–126.
30. Gunther AL, Remer T, Kroke A, Buyken AE. Early protein intake and later obesity risk: Which protein sources at which time points throughout infancy and childhood are important for body mass index and body fat percentage at 7 y of age? *Am J Clin Nutr* 2007;86:1765–1772.
31. Vang A, Singh PN, Lee JW, Haddad EH, Brinegar CH. Meats, processed meats, obesity, weight gain and occurrence of diabetes among adults: Findings from Adventist Health Studies. *Ann Nutr Metab* 2008;52:96–104.
32. Bagga D, Anders KH, Wang HJ, Glaspy JA. Long-chain N-3-To-n-6 polyunsaturated fatty acid ratios in breast adipose tissue from women with and without breast cancer. *Nutr Cancer* 2002;42:180–185.
33. Maillard V, Bougnoux P, Ferrari P, et al. N-3 and N-6 fatty acids in breast adipose tissue and relative risk of breast cancer in a case-control study in Tours, France. *Int J Cancer* 2002;98:78–83.
34. Marnett LJ. Oxy radicals, lipid peroxidation and DNA damage. *Toxicology* 2002;181–182:219–222.
35. Ray G, Batra S, Shukla NK, et al. Lipid peroxidation, free radical production and antioxidant status in breast cancer. *Breast Cancer Res Treat* 2000;59:163–170.
36. Boskou D. Olive oil. *World Rev Nutr Diet* 2000;87:56–77.
37. Owen RW, Giacosa A, Hull WE, Haubner R, Spiegelhalter B, Bartsch H. The antioxidant/anticancer potential of phenolic compounds isolated from olive oil. *Eur J Cancer* 2000;36:1235–1247.
38. Saarinen NM, Warri A, Airio M, Smeds A, Makela S. Role of dietary lignans in the reduction of breast cancer risk. *Mol Nutr Food Res* 2007;51:857–866.
39. Fink BN, Steck SE, Wolff MS, et al. Dietary flavonoid intake and breast cancer risk among women on Long Island. *Am J Epidemiol* 2007;165:514–523.
40. Velentzis LS, Cantwell MM, Cardwell C, Keshtgar MR, Leathem AJ, Woodside JV. Lignans and breast cancer risk in pre- and post-menopausal women: Meta-analyses of observational studies. *Br J Cancer* 2009;100:1492–1498.
41. Owen RW, Mier W, Giacosa A, Hull WE, Spiegelhalter B, Bartsch H. Phenolic compounds and squalene in olive oils: The concentration and antioxidant potential of total phenols, simple phenols, secoiridoids, lignans and squalene. *Food Chem Toxicol* 2000;38:647–659.
42. Covas M-I, Ruiz-Gutierrez V, de la Torre R, et al. Minor components of olive oil: Evidence to date of health benefits in humans. *Nutr Rev* 2006;64:S20–S30.
43. Newmark HL. Squalene, olive oil, and cancer risk. Review and hypothesis. *Ann NY Acad Sci* 1999;889:193–203.
44. Newby PK, Tucker KL, Wolk A. Risk of overweight and obesity among semivegetarian, lactovegetarian, and vegan women. *Am J Clin Nutr* 2005;81:1267–1274.
45. Spencer EA, Appleby PN, Davey GK, Key TJ. Diet and body mass index in 38000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans. *Int J Obes Relat Metab Disord* 2003;27:728–734.
46. Krajcovicova-Kudlackova M, Babinska K, Valachovicova M. Health benefits and risks of plant proteins. *Bratisl Lek Listy* 2005;106:231–234.
47. Sabate J. The contribution of vegetarian diets to human health. *Forum Nutr* 2003;56:218–220.
48. van Gils CH, Peeters PH, Bueno-de-Mesquita HB, et al. Consumption of vegetables and fruits and risk of breast cancer. *JAMA* 2005;293:183–193.
49. Donaldson MS. Nutrition and cancer: A review of the evidence for an anti-cancer diet. *Nutr J* 2004;3:19.
50. Tamimi RM, Hankinson SE, Campos H, et al. Plasma carotenoids, retinol, and tocopherols and risk of breast cancer. *Am J Epidemiol* 2005;161:153–160.
51. Brown MJ, Ferruzzi MG, Nguyen ML, et al. Carotenoid bioavailability is higher from salads ingested with full-fat than with fat-reduced salad dressings as measured with electrochemical detection. *Am J Clin Nutr* 2004;80:396–403.
52. Fielding JM, Rowley KG, Cooper P, O'Dea K. Increases in plasma lycopene concentration after consumption of tomatoes cooked with olive oil. *Asia Pac J Clin Nutr* 2005;14:131–136.
53. Ryan M, McInerney D, Owens D, Collins P, Johnson A, Tomkin GH. Diabetes and the Mediterranean diet: A beneficial effect of oleic acid on insulin sensitivity, adipocyte glucose transport and endothelium-dependent vasoreactivity. *QJ Med* 2000;93:85–91.

Address correspondence to:
Mary M. Flynn, Ph.D., R.D., L.D.N.
The Miriam Hospital
164 Summit Avenue
Providence, RI 02906

E-mail: Mary_Flynn@brown.edu

