

EPIDEMIOLOGY

Association Between Dietary Fat and Breast Cancer in Puerto Rican Postmenopausal Women Attending a Breast Cancer Clinic

EMILY SANTIAGO, MS, LND*; MICHAEL J. GONZÁLEZ, DSc, PhD, FACN*;
MARÍA I. MATOS, MHSN, LND*; CYNTHIA M. PÉREZ, MS, PhD†.

Objective. A pilot case-control study was conducted to examine the possible association between dietary fat intake and the development of postmenopausal breast cancer.

Background. Studies regarding the association between dietary fat intake and the development of breast cancer among postmenopausal women are lacking in Puerto Rico.

Methods. Eighteen cases and eighteen controls were interviewed to obtain sociodemographic information, medical history and dietary fat intake. A semiquantitative food frequency questionnaire containing 67 food items was used to collect the dietary information.

Results. Unadjusted odds ratios (OR) and their 95% confidence intervals (CI) showed a non-significant

positive association for total fat intake and the development of postmenopausal breast cancer (OR=1.57; 95% CI:0.42-5.90, p=0.25). The same non significant positive association was found for saturated fat intake (OR=1.57; 95% CI:0.42-5.90, p=0.25). Polyunsaturated fat (OR=1.25; 95% CI:0.34-4.64, p=0.37) and monounsaturated fat (OR=1.25; 95% CI:0.34-4.64, p=0.37) were also positively associated with postmenopausal breast cancer, although the associations were not statistically significant.

Conclusions. These results are consistent with other case-control studies that have shown non-significant positive associations between total fat and the different components of dietary fat and postmenopausal breast cancer. *Key words:* Breast cancer, Dietary fat intake, Case-control study, Postmenopausal women.

The relationship between dietary fat and cancer was first described by Tannenbaum in 1942 (1). Among the cancer anatomical sites most related to dietary fat intake is breast cancer (2). Results from epidemiologic and animal studies have shown a relationship between the amount and the level of saturation of dietary fatty acids and breast cancer risk. In general, the greater the amount of dietary fat, the greater the risk of breast cancer (3-5). Analysis of ecologic and case-control studies regarding the saturation of fat and breast

cancer risk show evidence of a positive association (3-4). Findings about the role of polyunsaturated fatty acids show a weak positive association in case-control studies (4), and a strong positive association in ecologic studies (3). For monounsaturated fat, the association has been found to be positive in case-control studies, but ecological studies show no evidence of an association (3). Evidence from animal studies using different rodent models shows that saturated fatty acids do not significantly enhance tumor growth, while polyunsaturated fatty acids can act as promoters, significantly enhancing tumor growth and progression (5). Results from epidemiologic studies of monounsaturated fatty acids and breast cancer have been variable (5).

The United States government has recommended that investigations related to diet and cancer should include studies of the relationship between specific components of dietary fat and cancer etiology (6). The purpose of this pilot study was to investigate the relationship of total, saturated, monounsaturated and polyunsaturated fat

*Department of Human Development, Nutrition Program and †Department of Biostatistics and Epidemiology, Graduate School of Public Health, University of Puerto Rico, Medical Sciences Campus.

Address for correspondence: Cynthia M. Pérez-Cardona, MS, PhD, Department of Biostatistics and Epidemiology, Graduate School of Public Health, University of Puerto Rico, Medical Sciences Campus, PO Box 365067, San Juan, Puerto Rico 00936-5067.

intakes with breast cancer in postmenopausal women. The specific objectives were to describe the sociodemographic characteristics of breast cancer cases and controls, to describe the distribution of fat components in cases and controls, and to estimate the magnitude of the association between postmenopausal breast cancer and polyunsaturated fat, monounsaturated fat, saturated fat, and total fat intakes.

Methods

All female patients of the Breast Cancer Clinic of the University Hospital, Puerto Rico Medical Center, that had a positive diagnosis of breast cancer between January 1992 through October 1994 were potential participants for the study. The log books of the Breast Cancer Clinic revealed there were 113 patients who were diagnosed during this period. Permission was obtained to review the medical records of the 113 patients in order to evaluate the pathology report, selection criteria and to obtain their addresses and phone numbers. The information was collected in standardized forms that were later used to select the participants.

The study group was comprised of the first 25 patients that fulfilled the eligibility criteria when reviewing the information gathered from the medical records. The eligibility criteria for the cases were: a positive breast cancer diagnosis between January 1992 and October 1994 and to have naturally reached menopause. Patients with a previous diagnosis of breast cancer were excluded from the study. Cases were contacted by phone and asked to participate in a nutrition study. A meeting was arranged to conduct a personal interview with those who agreed to participate. Among the 25 selected cases, 1 refused to participate, 2 could not be contacted, 2 were dead, 1 interview was not completed for fat intake and 1 was eliminated because during the interview she mentioned that she had stopped menstruating due to a total hysterectomy. Cases were asked to mention the name and phone number of a friend or neighbor who met the following characteristics: (1) no history of breast cancer, and (2) had reached menopause naturally. A total of 18 cases and 18 controls were interviewed.

A questionnaire was designed in order to collect information about sociodemographic characteristics, breast cancer risk factors and usual food intake. A pilot study was conducted to evaluate the adequacy of the questionnaire in the following areas: question sequence, question difficulty, administration time, coding, food list, and use of food models. Ten breast cancer patients with similar characteristics to the proposed study sample were interviewed the day of their follow-up appointments in

the Tumor and Breast Cancer Clinics at the University Hospital of Puerto Rico Medical Center, and appropriate changes were performed to the questionnaire. The pre-tested questionnaire contained four main sections:

1. sociodemographic information
2. reproductive history
3. personal and family history of cancer
4. dietary history

The interviews had a duration of approximately 45 minutes and were undertaken at the participants' homes. Before starting the interview the participants were asked to read and sign a consent form. In the dietary history section, cases were asked about their dietary patterns two years prior to the breast cancer diagnosis. Controls were asked about their dietary patterns two years prior to the interview. The dietary history was comprised of two sections: a twenty-four hour recall of past intake and a semiquantitative food frequency questionnaire. The twenty-four hour recall was used as a strategy to improve recall by the methods of categorization and reconstruction (7). To reconstruct the time of recall, participants were told to remember special events that occurred in the recall year, their occupation, and the location, time of day and companions at each meal. The twenty-four hour recall also served to cross check information with the food frequency questionnaire, and therefore improve data recollection. Food models (Nasco West, Fort Atkinson, WI) and household measures were used to determine usual portion sizes, and also as recall aids.

The food frequency questionnaire included 67 food items considered fat sources among commonly consumed foods in Puerto Rico (8). These foods were grouped into 9 categories: Dairy products, Meat, Poultry, Fish and Shell, Cured meats, Fritters, Farinaceous, Miscellaneous and Fats. The consumption of avocado was also included in the analysis, as well as the consumption of potato, green plantain and ripe plantain because they are usually prepared with fat. Avocado was treated like a seasonal fruit for the analysis. Its reported frequency of intake was multiplied per time of availability (9), and the result was used for nutrient calculation. Several high fat foods that were not included in the food frequency questionnaire were reported as part of the usual diet and were included in the analysis. If a food item was not available in the data bank, the food recipe was analyzed. If the software did not provide for the analysis of fat used in preparation of a specific food item, the recipe was also used to calculate the fat content of the reported portion. Nutrient daily average intake was determined from the food frequency questionnaire using the Minnesota Nutrition Data System (NDS 32) software, version 2.8, developed by the Nutrition Coordination Center (NCC) of the

University of Minnesota in Minneapolis (Food Database version 10A; Nutrient Database version S25) (10). If an analytic value is not available for a nutrient in a food item, NCC calculates the value based on the nutrient content of other nutrients in the same food item or on a product ingredient list, or estimates the value based on the nutrient content of similar foods. A missing value is allowed only if: a) the value is believed to be negligible, b) the food is usually eaten in very small amounts, c) it is unknown if the nutrient exists in the food at all, or d) there is no way to estimate the value because the food is unlike any other. Relative frequencies were used for each category of frequency of intake in the nutrient analysis.

Epi-Info version 6.04 (11) was used for data entry and, statistical analyses were performed using the SAS/STAT (12) software. Continuous variables were compared by means of Student's t test or Wilcoxon two-sample test, when appropriate. Categorical variables were compared by means of Yate's chi-square test or Fisher's exact test, when appropriate. Unadjusted odds ratios (OR) and test-based 95% confidence limits (95% CI) were calculated to estimate the magnitude of the associations among breast cancer and total fat, saturated fat, polyunsaturated fat, and monounsaturated fat intakes. All statistical tests were two-sided.

Results

Table 1 outlines the distribution of sociodemographic variables and conventional risk factors for breast cancer by case-control status. No significant differences ($p > 0.05$) were observed for age, marital status, educational level, age at menarche, age at menopause, parity, age at first birth, ovary removal, family history of breast cancer, oral contraceptive use, hormone use, smoking status and alcohol consumption. However, a lower proportion of cases lived in urban areas (22.2% vs. 61.1%, $p = 0.04$).

A summary of the mean intakes (g/day) of total fat, saturated fat, monounsaturated fat and polyunsaturated fat for cases and controls is given in Table 2. Cases showed a greater median intake for total fat and polyunsaturated fat (74.8 g/day, 13 g/day, respectively) than controls (64.3 g/day, 11.9 g/day, respectively), but these differences did not reach statistical significance ($p > 0.05$). Cases showed similar mean intakes for saturated fat and monounsaturated fat (27.8 ± 12.5 g/day, 27.4 ± 11.8 g/day, respectively) as controls (26.8 ± 12.6 g/day, 28.4 ± 12.4 g/day, respectively) but these differences were not statistically significant ($p > 0.05$).

Table 3 shows the associations between the specific dietary fat components and breast cancer risk. We calculated the controls' median intake for total fat,

Table 1. Sociodemographic Characteristics and Conventional Risk Factors for Breast Cancer by Case-Control Status.**

Variable	Cases		Controls		P value
	n	%	n	%	
Age \geq 65 years	8	44.4	5	27.8	0.49
Never being married	3	16.7	1	5.6	0.60
Years of education \geq 13	0	0.0	3	16.7	0.23
Urban area of residence	4	22.2	11	61.1	0.04
Age at menarche \leq 11 years	3	16.7	6	33.3	0.44
Age at menopause \geq 50 years	9	50.0	9	50.0	0.74
Never had children	4	22.2	2	11.1	0.65
Age at first birth \geq 30 years*	2	14.3	2	12.5	0.69
Positive history of ovary removal	0	0.0	1	5.6	1.00
Positive family history of breast cancer	2	11.1	1	5.6	1.00
Ever used oral contraceptives	3	16.7	8	44.4	0.15
Ever used hormones†	2	11.1	6	35.3	0.19
Ever smoked	6	33.3	7	38.9	1.00
Ever consumed alcohol	8	44.4	11	61.1	0.50

*There were four missing values among cases and two missing values among controls.

†There was one missing value among controls.

**Breast Cancer Clinic, University Hospital, San Juan, Puerto Rico, 1995.

saturated fat, polyunsaturated fat and monounsaturated fat, and used the levels ≤ 64.3 g/day, ≤ 24.0 g/day, ≤ 24.4 g/day, and ≤ 11.9 g/day, respectively, as the reference categories. Results showed a non-significant positive association between postmenopausal breast cancer and total fat intake (OR=1.57; 95% CI:0.42-5.90, $p = 0.25$). The same non-significant positive association was found for

Table 2. Mean Intake (g/day) of Specific Dietary Fat Components by Case-Control Status**

Nutrient	Cases	Controls	P value
Total fat	74.2 \pm 28.6	75.1 \pm 34.6	0.79*
Saturated fat	27.8 \pm 12.5	26.8 \pm 12.6	0.81†
Polyunsaturated fat	13.8 \pm 5.9	14.4 \pm 8.8	0.84*
Monounsaturated fat	27.4 \pm 11.8	28.4 \pm 12.4	0.79†

*P value are based on Mann-Wilcoxon two samples test for comparison of medians.

†P value are based on Student's test for comparison of means.

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saturated fat intake (OR=1.57; 95% CI:0.42-5.90, p=0.25). Similarly, polyunsaturated fat and monounsaturated fat showed non-significant positive associations with breast cancer risk (OR=1.25; 95% CI:0.34-4.64, p=0.37).

Table 3. Association Between Specific Dietary Fat Components and Breast Cancer**

Nutrient	OR*	95% CI*	P value
Total fat			
>64.3 g/day	1.57	0.42-5.90	0.25
≤64.3 g/day	1.00	-	
Saturated fat			
>24.0 g/day	1.57	0.42-5.90	0.25
≤24.0 g/day	1.00	-	
Polyunsaturated fat			
>24.4 g/day	1.25	0.34-4.64	0.37
≤24.4 g/day	1.00	-	
Monounsaturated fat			
> 11.9 g/day	1.25	0.34-4.64	0.37
≤11.9 g/day	1.00	-	

* Odds ratio and 95% confidence interval

** Breast Cancer Clinic, University Hospital, San Juan, Puerto Rico, 1995.

Discussion

Several mechanisms of action have been proposed to support the link between dietary fat and breast cancer. Among them are: lipid peroxidation, activation of oncogene expression, mediation by metabolites of fatty acids, alterations of the endocrine system, membrane alterations, changes in immune function, caloric consumption and intercellular communication (13). However, while results from ecologic studies are consistent to support the link between dietary fat and breast cancer (3), case-control and cohort studies have failed to consistently show an association (14), probably due to methodological problems (15). The inconsistency and contradictory results in epidemiologic studies and experimental rodent models have not allowed a complete understanding of the role of dietary fat in breast cancer development.

The only current dietary recommendation to lower cancer risk regarding fat intake is to lower total fat and saturated fat ingestion to less than 30% and 10% of total kilocalories, respectively (16). Evidence from some animal studies suggest that a threshold level for breast cancer development exists between 5% and 25% wt/wt, around 10%-40% kilocalories from fat (5,17). This suggestion is supported by the fact that although total fat intake in the US population has decreased in the last decades (18), breast cancer incidence rates have increased and mortality rates have remained constant (19). This observation is also supportive of a positive association for polyunsaturated fatty acids because although total fat intake shows a decline, the proportion of linoleic acid in the US diet has been increasing since 1950 (18). The increase in incidence rates is mostly due to an increase in incidence rates in women 65 years and older (19). This population group is also the one who has shown to have the strongest positive association between fat intake and breast cancer risk in ecologic (3) and case control studies (4).

A recent report from the Puerto Rico Department of Health shows that breast cancer is among the five most frequent sites of cancer for women of all ages (20). Moreover, breast cancer is the leading cause of death for women between ages 40 to 59 (20,21). Its trends have shown increasing incidence rates since 1955, and it has been estimated that incidence rates will continue to increase (20). Although much progress has been made in diagnosis, mortality rates during the past 20 years have remained constant in the United States (19). In Puerto Rico, mortality rates have been increasing since 1950 (20).

Dietary intakes of total fat, polyunsaturated fat, saturated fat and monounsaturated fat showed non-significant positive associations with postmenopausal breast cancer risk in this study. These findings are congruent with that of the combined analysis in that all four fats that were analyzed showed positive associations with postmenopausal breast cancer risk (4). In both studies total fat and saturated fat showed the greatest positive effect compared to monounsaturated and polyunsaturated fat intake. Moreover, we found the same magnitude of the odds ratio for polyunsaturated fat intake (OR=1.25), although it was not statistically significant.

Our study findings also agree with results from ecologic studies that have found positive associations for total, saturated and polyunsaturated fat, with the difference that no association was observed for monounsaturated fat (3,22). In contrast, results from cohort studies are not supportive of a relationship between fat intake and breast cancer risk. A recent pooled analysis of the primary data of seven cohort studies showed no evidence between total

fat, and the risk of postmenopausal breast cancer (RR=1.01; 95% CI:0.91-1.12) in 3,465 patients (23). Although this study was carefully designed in order to correct deficiencies of previous cohort studies, its results are not free from errors in dietary intake measurements. Data from all epidemiologic designs that make use of food frequency questionnaires or 24-hour recalls (including this study) are measured with error in the dietary assessment. Food frequency questionnaires have major limitations inherent to its design. Inaccuracies are a result of errors in estimating usual size of intake, frequency of consumption, and incomplete listing of foods. Validation studies to correct errors from dietary assessment conducted with food frequency questionnaires are performed using either dietary records or 24-hour recalls. These methods are themselves subject to errors because participants may report inaccurate food intakes for reasons related to memory, the interview situation, the inability to quantify portion sizes, and may not represent the time period of interest. These errors can result in an underestimation of nutrient intake by 20% (24). It has been suggested that the appropriate validation study for nutrient intakes calculated from a food frequency questionnaire would require a nonintrusive observation of the participant's dietary intake for a long period of time (25). Therefore, neither case-control studies or cohort studies are free from errors in the measurement of dietary variables.

Cases and controls showed greater mean total fat (74.2 g/day and 75.1 g/day, respectively) and saturated fat intake (27.8 g/day and 26.8 g/day, respectively) compared to mean total fat (57.0 g/day) and saturated fat (19.2 g/day) intake of women aged 40 years and older in the Third National Health and Nutrition Examination Survey (26). These results could indicate that although fat intake in the United States has been showing a decline from 40.6% in 1960 (11) to 33.9% between 1988 and 1991 (26), the Puerto Rican population may not be meeting the recommendations of lowering fat intake. There is evidence that shows that the fat intake in the Puerto Rican diet is related to socioeconomic status (27). In general, the higher the socioeconomic status, the higher the fat content in the diet. Since the population of this study is characterized by low socioeconomic level, it can be deduced that the fat intake in populations of higher socioeconomic levels may be even higher.

It is important to mention that in animal studies the effect of dietary fat on the development of breast cancer have been shown to be greater in the promotion stage of the tumorigenic process. Although a causal relationship cannot be discarded, most of the proposed mechanisms of dietary fat on breast cancer development take action in

the promotion stage, and not in the initiation stage (for a review see reference 6). The failure of case-control studies to demonstrate a definitive relationship between the development of postmenopausal breast cancer and dietary fat intake, in addition to their limitations, may be because this analytical design evaluates hypotheses of causal relationships (28) and therefore does not evaluate the effect of dietary fat on the progression of the disease, where dietary fat may have greater effect.

As an observational study, this case-control study has several limitations. First, we were unable to adjust for non-dietary covariates due to the small sample size achieved. Second, the use of friends and relatives as a source of controls in studies concerning dietary factors could underestimate the true magnitude of the association between fat and breast cancer risk due to similar exposures (29). Third, measurement error in the assessment of covariates may have resulted in residual confounding. Fourth, caloric intake was not evaluated. Although several studies have ruled out the possible effect of total caloric intake and calories from fat in the development of postmenopausal breast cancer (4,6), it would have been interesting to analyze what percentage of calories from total fat, saturated fat, monounsaturated fat and polyunsaturated fat does the corresponding mean fat intake represent.

Conclusions

Our findings agree with results from the meta-analysis of the original data of 12 case-control studies conducted by Howe et al. (4). Non-significant positive associations were found for total, saturated, monounsaturated, and polyunsaturated fat intakes, being stronger for total and saturated fats. These findings are also in agreement with results from ecologic studies but not with results from cohort studies.

Epidemiological studies that measure the effect of dietary variables on the development of disease could not only be biased because of errors inherent to each epidemiological design, but could also be biased because of errors in measuring dietary variables. These methodological problems, plus the fact that dietary fat has shown to have greater effect on the promotion stage of the tumorigenic process and, both case-control and cohort studies have focused on a causal relationship, may account for the inconsistency in the results of epidemiological studies.

Mean values for total and saturated fat intake of cases, controls and the entire population were higher compared to the mean values for total and saturated fat intake of the US female population of the same age groups (26).

These findings suggest that although there has been a decline in mean total fat and saturated fat intake in the US population, dietary fat intake patterns in Puerto Rico may be different (26). Some recommendations should be made:

1. Undertake this study using a greater number of participants to evaluate the effect of potential confounding variables on the dietary fat and breast cancer association.
2. Determine mean nutrients intakes of the Puerto Rican population by age and gender groups in order to a) correlate changes in food intake with incidence and mortality rates, b) evaluate educational programs, c) have reference data to compare future studies and, d) evaluate the achievement of nutritional objectives for the year 2000.
3. Follow the actual dietary recommendations regarding fat intake in order to lessen the possible risk associated to breast cancer development and other types of cancer, while definitive conclusions can be made.
4. Design and conduct controlled studies to evaluate the relationship of dietary fat and its different components on the progression of breast cancer through the analysis of occurrence of metastasis and survival.

Resumen

Se realizó un estudio piloto caso-control para evaluar la relación entre consumo de grasa en la alimentación y el desarrollo de cáncer de mama después de la menopausia. Se entrevistaron 18 casos y 18 controles para obtener información sociodemográfica, historial médico y consumo de grasa en la alimentación. La razón de productos cruzados (OR) mostró asociaciones positivas no significativas para el consumo total de grasa y la grasa saturada con el desarrollo de cáncer de mama (OR=1.57, 95% CI: 0.42-5.90, p=0.25). La grasa poliinsaturada y la grasa monoinsaturada (OR=1.25; 95% CI:0.34-4.64, p=0.37) se asociaron positivamente con el desarrollo de cáncer de mama pero no alcanzaron significancia estadística. Estos resultados son consistentes con estudios de casos y controles previos que han demostrado asociaciones positivas no significativas entre la grasa en la alimentación y el desarrollo de cáncer de mama después de la menopausia.

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