Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Difference in fatty acids composition of breast adipose tissue in women with breast cancer and benign breast disease

Diferencia en la composición de ácidos grasos del tejido adiposo de la mama en mujeres con cáncer de mama y enfermedad benigna de la mama

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Abstract

Introduction: Breast cancer is the second most common cancer in the world, and the most frequent cancer among women. Moreover, there are factors that influence the risk for breast cancer including the age, genetic and endocrine factors, and lifestyle.

Objectives: To evaluate the consumption of fatty acids; compare the fatty acids composition in the breast adipose tissue of women with breast cancer and benign breast disease as well as potential risk factors; and describe the genotypic frequency of the Pro12Ala PPARγ polymorphism.

Material and methods: A hospital-based case-control study was conducted including incident cases ($n = 38$ breast cancer; $n = 75$ benign breast disease; $n = 166$ control). Lifestyle features, socioeconomic issues, dietary intake, anthropometry, and blood and tissue data were assessed.

Results: No differences were observed for fatty acids intake. Interestingly, lauric acid ($p = 0.001$), myristic acid ($p = 0.036$), stearic acid ($p = 0.031$), and total saturated fatty acids (SFAs) ($p = 0.048$) had lower concentrations in BC than in BBD women, while palmitoleic acid ($p = 0.022$), erucic acid ($p = 0.002$), total monounsaturated fatty acids (MUFAs) ($p = 0.039$) and oleic acid/stearic acid ratio ($p = 0.015$) increased. There was no significant association between PPARγ polymorphism and studied groups ($p = 0.977$). The age at first full pregnancy ($p = 0.004$) was significantly associated with the development BC, whereas BMI ($p = 0.005$); percentage of body fat ($p = 0.024$); physical activity ($p = 0.036$); and age at menarche ($p = 0.008$), at first full pregnancy ($p < 0.001$), and of first mammogram ($p = 0.018$) were significantly associated with the development of BBD.

Conclusion: The results suggest a different fatty acids composition of breast adipose tissue, a biomarker of long-term dietary intake, particularly for SFAs, MUFA and 18: 1 n-9/18: 00 ratio. Our findings also show that are differences in the factors related to the development of BC and BBC.

Resumen

Introducción: el cáncer de mama (CM) es el segundo cáncer más común en el mundo, y el cáncer más frecuente entre las mujeres. Por otra parte, hay factores que influyen en el riesgo de padecer CM, entre los que se encuentran la edad, factores genéticos y endocrinos, y el estilo de vida.

Objetivos: evaluar el consumo de ácidos grasos; comparar la composición de ácidos grasos en el tejido adiposo de mama de las mujeres con CM y enfermedad benigna de mama (EBM), así como los posibles factores de riesgo; y describir la frecuencia genotípica del polimorfismo Pro12Ala PPARγ.

Material y métodos: se llevó a cabo un estudio caso-control basado en hospitales, incluyendo casos incidentes (n = 38 cáncer de mama, n = 75 enfermedad benigna de mama, n = 166 control). Se evaluaron las características del estilo de vida, las cuestiones socioeconómicas, la ingesta dietética, la antropometría y los datos de sangre y tejidos.

Resultados: no se observaron diferencias para la ingesta de ácidos grasos. Curiosamente, ácido láurico (p = 0,001), ácido mirístico (p = 0,036), ácido esteárico (p = 0,031) y los ácidos grasos totales saturados (AGS) (p = 0,048) tenían concentraciones más bajas en CM que en mujeres EBM, mientras ácido palmitoleico (p = 0,022), ácido erúcico (p = 0,002), los ácidos totales grasos monoinsaturados (MUFA) (p = 0,039) y la relación ácido oleico/ácido esteárico (p = 0,015) aumentó. No hubo asociación significativa entre el polimorfismo PPAR gamma y los grupos de estudio (p = 0,977). La edad al primer embarazo (p = 0,004) se asoció de forma significativa con el desarrollo de CM, mientras que el IMC (p = 0,005), porcentaje de grasa corporal (p = 0,024), la actividad física (p = 0,036) y la edad de la menarquia (p = 0,008), al primer embarazo (p < 0,001), y de la primera mamografía (p = 0,018), fueron significativamente asociados con el desarrollo de EBM.

Conclusiones: los resultados sugieren una composición diferente de ácidos grasos del tejido adiposo de la mama, un biomarcador de la ingesta dietética a largo plazo, particularmente para SFA, MUFA y 18: 1 n-9/18: 00. Nuestros hallazgos también muestran que existen diferencias en los factores relacionados con el desarrollo de CM y EBM.

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INTRODUCTION

Breast cancer (BC) is the second most common cancer in the world, and the most frequent cancer among women (1). There are several recognized risk factors for BC, mainly age, genetic and endocrine factors, and lifestyle (2). It is estimated that up to 35% of risk factors are associated with diet (3).

However, the assessment of the association of diet components with BC risk is not an easy task because of the limitations of conventional methods to assess dietary intake, such as memory, difficulty in estimating portion size, day-to-day variability, seasonal eating patterns, and use of the food consumption tables (4,5). In fact, the determination of tissue nutrients may provide a more accurate estimate of dietary intake. The fatty acid (FA) content of the adipose tissue has been proposed as a biomarker of FA intake most appropriate because it reflects the long-term ingestion, up to 2 years previous, when no severe weight loss had occurred (6).

The peroxisome proliferator-activated receptor gamma (PPARγ) has been shown to be important in many biochemical functions such as the adipocyte differentiation and also act as a tumor suppressor gene, inhibiting the growth of several cell types, and induction of apoptosis (7). However, until this moment, studies investigating the association between PPARγ polymorphism and the risk of BC reported inconclusive results (8-14).

Overall, the aims of this study were to evaluate the consumption of fatty acids; to compare the fatty acids composition of the breast adipose tissue of women with BC and benign breast disease (BBD); to identify factors associated with risk of developing of BC and BBD; as well as to describe the genotypic frequency of PPARγ Pro12Ala polymorphism.

MATERIALS AND METHODS

SAMPLE STUDY

This is a double-blind, hospital-based, case-control study conducted with women attending the mastology and/or gynecology service of a public hospital in Belo Horizonte, Brazil. All women attended between January and July 2006 was invited to participate in the study. In this study, we included only women without previous diagnosis of BC or BBD. The volunteers were divided in three groups: case, women with histological diagnosis of malignant breast disease; BBD, women diagnosed with fibrocystic breast changes or other non-proliferative BBD; and Control (C) women who underwent a routine examination or gynecological surgery and had a recent mammogram result. The final sample was composed of 229 women. Written consent was given by all women after they had been informed of the objective and protocol of the study. The study followed principles of the Declaration of Helsinki and was approved by the National Committee of Ethics in Research (protocol number: 1889/2005).

DATA COLLECTION

Information about lifestyle, as well as gynecological and obstetric history, and socioeconomic issues were collected using a previously validated questionnaire for the population of the region studied (15). Dietary intake was assessed using a semiquantitative food frequency questionnaire (SFFQ).

Volunteers who consumed at least 1 dose (10 g of alcohol) of any alcoholic beverage/day or in a frequency of more than 3 days/week were considered alcoholic (16). In the same way, who smoked at least 1 cigarette per day, regardless of the time of use were considered smokers. Physical activity was assessed using the short version of international physical activity questionnaire (IPAQ) (17).

Anthropometric measurements such as weight, height, waist, and hip circumference were obtained from all the participants according to the standard protocol (18-20). The waist to hip ratio (WHR), waist to height ratio (WHtR), and body mass index (BMI in kg/m^2) were calculated. Overweight and obesity were defined as BMI ≥ 25.0 to 29.9 kg/m^2 and ≥ 29.9 kg/m^2, respectively (21).

Moreover, the total body fat (%) was estimated by bioelectrical impedance vertical Tanita® (ModelTBF 531, Tanina Corporation of America, Illinois, USA) and classified by Gallagher et al. (22).

The collection of biological material occurred on the day of surgery after 12 h fasting. Blood and breast adipose tissue samples were collected and immediately protected from light and stored in liquid nitrogen at -80 °C until the time of analysis.

FATTY ACIDS IN BREAST ADIPOSE TISSUE

The lipids of the breast adipose tissue were extracted by Folch (23) methodology and saponified and esterified according to Hartmann and Lago (24). The FA methyl esters were identified by gas chromatography (CG-17A Shimadzu®/Class model) (25). Peak identification was made by comparison of their retention times with that of a mixture of commercial standards (FAME mix, Supelco®, USA). FA composition was expressed as percentage of the lipid fraction relative to the total FA content of the sample.

GENOTYPING

Genomic DNA was obtained from stored buffy coat. Briefly, buffy coats were digested using lysing solution, Madissen (0.1M Tris-HCl pH = 8.0; 0.4 M EDTA; 0.2% SDS; 1M NaCl; pH = 8.0), followed by addition of proteinase K (20 mg/mL) and incubated overnight at 37 °C. Then, the DNA was precipitated with saturated phenol and chloroform:isoamyl alcohol (24:1). Finally, cold isopropyl alcohol was added and homogenized slowly until the precipitation of DNA, which was dried at room temperature.

To detect the presence the proline 12 alanine (Pro12Ala) polymorphism, a 257-bp fragment of the PPARγ gene was selectively amplified by PCR (26). The amplified fragment was digested with the restriction enzyme BstU-I according to manufacturer's instruc-

tions (Promega®, Madison, WI, USA), and the products of digestion were analyzed in polyacrylamide gel. The genotyping of patients were determined as follows: a single 257 bp fragment for the CC (Ala12Ala) genotype; two fragments of 223 and 34 bp for the GG (Pro12Pro) genotype; and three fragments of 257, 223, and 34 bp for the CG (Pro12Ala) genotype.

STATISTICAL ANALYSES

Normal distribution of data was determined by Kolmogorov-Smirnov test. The Kruskal-Wallis and analysis of variance (ANOVA) was used to determine the differences in median and mean values, respectively, between the BC, BBD, and C groups. Associations between categorical variables were tested by Pearson's chi-squared test, and when necessary the chi-square partition test with Bonferroni correction was utilized. Odds Ratio and 95% confidence intervals for risk of BC and BBD were examined using multinomial logistic regression. Initially, we applied simple multinomial logistic regression and the independent variables with significance < 0.20 were considered as candidates for the final model. Then, multiple multinomial logistic regressions were conducted in which the variables remained with a final model with significance level of $\alpha \leq 0.05$.

The food consumption data were log-transformed before statistical analyses, and the data were adjusted by energy according to the residual model (27).

Hardy-Weinberg Equilibrium was tested to compare the observed with expected genotype frequencies. Frequencies of the genotypes of PPARγ polymorphism between the study groups was performed by the chi-square test. All analyses were conducted in SPSS® software, version 20.

RESULTS

The anthropometric, clinical, sociodemographic and lifestyle characteristics of BC, BBD, and C are described in table I. As it can be seen, the median age was higher in BC group (p < 0.001), and they made less use of oral contraceptives (p = 0.011). Furthermore, when compared to BBD group, women with BC had made their first mammogram (p < 0.001) at a later age and presented menopause at an older age too (p = 0.037) suggesting a longer interval between ages at menarche and natural menopause.

However, in control group, women had the first full pregnancy younger (p < 0.001). While women without the disease had breastfed more (p < 0.001), had no family history of breast cancer (p < 0.001), or previous history of benign breast lesion (p < 0.001). The others parameters did not differ between the study groups.

In relation to food consumption, no differences were observed between the three evaluated groups (Table II). However, the composition of fatty acids from the breast adipose tissue was different between groups (Table III). The tissue concentration of lauric acid, myristic acid, stearic acid, and total saturated fatty acids (SFAs)

Table I. Anthropometric, clinical, sociodemographic, and lifestyle characteristics of study participants, by groups

Variables	Groups			p
	BC (38)	BBD (75)	C (116)	
Age (years)	53 ± 26[a]	43 ± 22[b]	47 ± 10[c]	< 0.001[*♦]
BMI (kg/m²)	27.51 ± 6.50[a]	24.48 ± 4.64[b]	27.33 ± 5.40[a]	0.001[**■]
WHR	0.88 ± 0.08	0.85 ± 0.06	0.87 ± 0.07	0.058[**]
WhtR	0.59 ± 0.10[a]	0.52 ± 0.07[b]	0.57 ± 0.08[a]	0.001[**■]
Total body fat (%)	33.47 ± 9.23	31.30 ± 7.93	34.16 ± 7.95	0.063[**]
Age at menarche (years)	13.00 ± 2.00	12.00 ± 3	13 ± 2	0.134[*]
Age at menopause (years)	48.9 ± 5.46[a]	44.32 ± 7.57[b]	46.66 ±5.05[ab]	0.037[**■]
Age at first full pregnancy (years)	24.50 ± 12.00[a]	24.00 ± 8.0[a]	21.00 ± 6.00[b]	0.001[*♦]
Age of first mammogram (years)	43.0 ± 15.00[a]	39.0 ± 31[b]	40.0 ± 9.00[ab]	< 0.001[*♦]
Breast feeding (yes, %)	24 (63.15)[a]	36 (48.00)[a]	96 (82.75)[b]	< 0.001[***♯]
Nulliparity (yes, %)	14 (36.84)[a]	28 (37.33)[a]	11 (9.48)[b]	< 0.001[***♯]
Oral Contraceptive use (yes, %)	14 (36.84)[b]	48 (64)[a]	72 (62.06)[a]	0.011[***♯]
Hormone replacement therapy (yes, %)	5 (13.15)	8 (10.66)	16 (13.79)	0.814[***]
Live in countryside (yes, %)	13 (34.21)[b]	53 (70.66)[a]	74 (63.79)[a]	0.0004[***♯]
Per capita income (U$)	116.66 ± 111.09[a]	140.83 ± 103.12[b]	100.00 ± 118.33[a]	0.047[*♦]
Educational level (n, %)	37	74	116	0.067[***]
Primary	26 (70.27)	40 (54.05)	86 (74.13)	

(Continuation in the next page)

Table I (Cont.). Anthropometric, clinical, sociodemographic, and lifestyle characteristics of study participants, by groups

Variables	Groups			p
	BC (38)	BBD (75)	C (116)	
Secondary	10 (27.03)	29 (39.18)	25 (21.55)	
University/Post-graduation	1 (2.70)	5 (6.77)	5 (4.32)	
Physical activity (n, %)				0.088***
Sedentary	20 (52.63)	36 (48.00)	41 (35.34)	
Light	15(39.47)	24 (32.00)	56 (48.27)	
Moderate	3 (7.90)	15 (20.00)	19 (16.37)	
Smoking (yes, %)	3 (7.90)	12 (16.00)	19 (16.37)	0.407***
Alcool intake (g/day)	4.2 ± 13.69	3.63 ± 9.79	6.13 ± 17.86	0.218*
Family history of breast cancer (yes, %)	10 (26.31)[a]	13 (17.33)[a]	0[b]	< 0.001***•

BC: breast cancer; BBD: benign breast disease; C: control group; BMI: body mass index; WHR: waist to hip ratio; WhtR: waist to height ratio *Kruskal-Wallis Test; **Oneway ANOVA; ■Tukey Test; ♦Dunn Test; ***Chi-Square Test; #Chi-Square partition Test with Bonferroni correction. •Fisher exact Test with Bonferroni correction. Values expressed as mean ± standard deviation for parametric variables and median and interquartile interval for non-parametric variables. Letters a, b and c when repeated in the same row represent absence of significant difference.

Table II. Consumption of specific fatty acids of study participants, by groups

Fatty acid intake (g/day)[a]	Groups			p*
	BC (38)	BBD (75)	C (116)	
12:0 (lauric acid)	0.27 (0.08-1,45)	0.29 (0.05-1.19)	0.18 (0.02-0.68)	0.059
14:0 (myristic acid)	0.90 (0.38-4.82)	1.29 (0.34-3.97)	0.94 (0.27-2.64)	0.477
16:0 (palmitic acid)	11.89 (5.15-19.12)	11.65 (7.40-20.76)	8.91 (5.00-15.70)	0.326
18:2 n6 (linoleic acid)	10.15 (7.47-15.41)	15.08 (10.20-24.34)	13.24 (7.10-25.08)	0.304
18:3 n3 (α-linolenic acid)	1.07 (0.77-1.61)	1.47 (0.89-2.70)	1.41 (0.74-2.79)	0.368
20:4 n-6 (arachidonic acid)	0.03 (0.00-0.09)	0.03 (0.01-0.12)	0.02 (0.01-0.07)	0.439
20:5 n-3 (eicosapentaenoic acid)	0.01 (0.00-0.02)	0.00 (0.00-0.02)	0.00 (0.00-0.02)	0.999
22:6 n-3 (docosahexaenoic acid)	0.01 (0.00-0.03)	0.01 (0.00-0.08)	0.01 (0.00-0.05)	0.663
Total SFAs	27.95 (11.16-44.45)	29.39 (18.50-59.23)	24.45 (12.53-39.60)	0.208
Total MUFAs	19.74 (12.57-39.12)	33.77 (18.25-62.24)	46.41 (14.41-49.55)	0.069
Total n-6 PUFAs	10.18 (7.49-15.41)	15.31 (10.20-24.40)	13.28 (7.22-25.16)	0.301
Total n-3 PUFAs	1.07 (0.76-1.59)	1.59 (0.92-2.66)	1.42 (0.76-2.75)	0.324
Total PUFAs	16.21 (10.85-26.37)	23.51 (14.87-35.93)	22.38 ± 25.98 n(12.86-38.83)	0.281
Total Lipids	77.60 (41.63-122.97)	87.69 (66.74-178.25)	73.62 ± 86.84 (43.73-130.56)	0.254

BC: breast cancer; BBD: benign breast disease; C: control group; PUFA: polyunsaturated fatty acids; MUFA: total monounsaturated fatty acids. ANOVA Test; [a]Fatty acid intake was adjusted by energy intake using residual model. Values are median (25th-75th quartile).

were lower in BC than in BBC, while palmitoleic acid, erucic acid, total MUFAs, and oleic acid/stearic acid ratio were higher in BC than in BBC, reinforcing the hypothesis regarding the necessity of balance in consumption of fatty acids in dietary lipids.

The observed frequency of genotypes was not different from the expected frequency demonstrating to be in Hardy-Weinberg equilibrium in this population. Moreover, no significant associ-ation was observed between PPARγ Pro12Ala polymorphism and studied groups (p = 0.977). The percentage of women with the genotype CG or GG was 17.4, 30.4, and 52.2%, in the BC, BBD, and C groups, respectively.

About the risk factors, it was observed that the age at first full pregnancy (p = 0.004) was highlighted in this study as an important factor associated with the development of BC. In addition, for women

Table III. Breast adipose tissue concentration of fatty acids in breast cancer and breast benign disease women

Variables	Groups		p
	BC (38)	**BBD (75)**	
	% of total fatty acids		**p**
12:0 (lauric acid)	0.16 ± 0.09	0.22 ± 0.16	0.001*
14:0 (myristic acid)	1.69 ± 0.42	1.88 ± 0.46	0.036**
15:0 (pentadecylic acid)	0.19 ± 0.06	0.18 ± 0.05	0.134**
16:0 (palmitic acid)	21.16 ± 1.45	21.52 ± 1.66	0.270**
17:0 (margaric acid)	0.27 ± 0.11	0.25 ± 0.10	0.597*
18:0 (stearic acid)	4.63 ± 1.35	5.22 ± 1.34	0.031**
20:0 (arachidic acid)	0.15 ± 0.06	0.16 ± 0.06	0.219**
21:0 (heneicosanoic acid)	0.24 ± 0.14	0.22 ± 0.15	0.397**
22:0 (behenic acid)	0.26 ± 0.10	0.28 ± 0.11	0.587**
23:0 (docosanecarboxylate acid)	0.45 ± 0.20	0.35 ± 0.13	0.029**
Total SFAs	28.81 ± 3.13	30.02 ± 4.46	0.048*
14:1 (myristoleic acid)	0.13 ± 0.07	0.12 ± 0.06	0.456*
16:1 n-7 (palmitoleic acid)	3.07 ± 1.38	2.65 ± 1.22	0.022*
17:1 (heptadecenoic acid)	0.22 ± 0.05	0.20 ± 0.06	0.054**
18:1 n-9 (oleic acid)	41.05 ± 2.45	40.02 ± 2.96	0.068
20:1 n-9 (gondoic acid)	0.55 ± 0.13	0.55 ± 0.12	0.954
22:1 n-9 (erucic acid)	0.32 ± 0.16	0.22 ± 0.12	0.002**
Total MUFAs	45.53 ± 3.27	43.96 ± 3.96	0.039*
20:1 n-9 (gondoic acid)	0.55 ± 0.13	0.55 ± 0.12	0.954
18:2 n-6 *trans* (rumenic acid)	0.15 ± 0.15	0.18 ± 0.16	0.261*
18:2 n-6 (linoleic acid)	22.77 ± 2.71	23.31 ± 3.92	0.397**
18:3 n-6 (λ-linolenic acid)	0.23 ± 1.12	0.38 ± 1.17	0.714*
20:2 n-6 (eicosadienoic acid)	0.29 ± 0.09	0.30 ± 0.08	0.765
20:3 n-6 (dihomo-γ-linolenic acid)	0.04 ± 0.06	0.04 ± 0.01	0.483*
20:4 n-6 (arachidonic acid)	0.04 ± 0.01	0.03 ± 0.01	0.265*
Total n-6 PUFAs	23.98 ± 2.95	24.26 ± 5.32	0.747*
18:3 n-3 (α-linolenic acid)	0.96 ± 0.28	1.03 ± 0.30	0.315**
20:3 n-3 (dihomo- α-linolenic acid)	0.40 ± 0.21	0.29 ± 0.18	0.065**
20:5 n-3 (eicosapentaenoic acid)	0.20 ± 0.12	0.16 ± 0.10	0.255**
22:6 n-3 (docosahexaenoic acid)	0.07 ± 0.03	0.06 ± 0.03	0.372**
Total n-3 PUFAs	*1.01 ± 0.77*	1.05 ± 0.74	0.757*
Total PUFAs	*25.11 ± 3.16*	*25.32 ± 5.06*	*0.865**
n-3/n-6 PUFA ratio	0.04 ± 0.02	0.04 ± 0.01	0.452**
20:4 n-6/20:3 n-6 ratio	0.88 ± 0.45	0.99 ± 0.09	0.551**
20:3 n-6/18:2 n-6 ratio	0.002 ± 0.00	0.002 ± 0.00	0.290*
18:1 n-9/ 18:0 ratio	8.921 ± 4.97	7.727 ± 2.69	0.015*

BC: breast cancer; BBD: benign breast disease; PUFA: polyunsaturated fatty acids. *Mann-Whitney Test; **T-Student Test.
Total SFAs: 10:0.12:0. 14:0. 15:0. 16:0. 17:0. 18:0. 20:0. 21:0. 22:0. 23:0. 24.0
Total MUFAs: 14:1. 16:1. 17:1. 18:1. 20:1. 21:1. 24:1n-9
Total PUFAs: 18:2n-6. 18:3n-6. 20:3n-6. 20:4 n-6. 18:3n-3. 20:3n-3. 20:5n-3. 22:6n-3
Total n-6 PUFAs: 18:2n-6. 18:3n-6. 20:3n-6. 20:4 n-6
Total n-3 PUFAs: 18:3n-3. 20:3n-3. 20:5n-3. 22:6n-3

with BBD, BMI ($p = 0.005$), total body fat ($p = 0.024$), physical activity ($p = 0.036$), and age at menarche ($p = 0.008$), at first full pregnancy ($p < 0.001$), and of first mammogram ($p = 0.018$) were pointed as risk factors for the occurrence of BBD (Table IV).

DISCUSSION

Great efforts have been made in the scientific community to improve our understanding of the factors associated with breast cancer (1). However, few studies assessed the BBD and its risk factors as well the behavior of this disease.

We found that women with BC had the menopause in older age. Recent study reported that women with the longest reproductive lifespan were 1.5-1.7 times more likely to have BC compared with women with the shortest reproductive lifespan (28).

However, in control group, women had the first full pregnancy at younger age, which is according to recent evidence to suggest that pregnancy at an early age has a strong protective effect against BC in humans, through changes in hormonal dynamics and pronounced changes in gene expression (29). In addition, in our study, the oral contraceptive use demonstrated a protective action, different from what has been described in the literature (30,31).

To our knowledge, this is the first case-control study that utilized WHtR as screening tool, and we found the difference between groups and WHtR. Recent evidence suggests that WHtR is a better measure of the health risk such as obesity and cardio-metabolic risk factors, wherein the larger the ratio the greater the risk.

In relation to the profile of fatty acid determined in patients with CA and DBM, our results were contrary to that described in the literature, and this can be possibly due to characteristics significantly different (Table I). Contrary to our results, concentrations of myristic acid were elevated in cancer breast tissue in Greek women (32). Greek patients with BC had significantly higher total MUFA ($p < 0.001$), lower total SFA ($p < 0.01$) in breast adipose tissue compared to patients with benign breast tumors, which is consistent with the present study (33). In addition, we suggest that the differences observed in this analysis of FA as biomarker intake (Table III), may occur due to differences in long-term food intake.

Our finding of a higher oleic acid/stearic acid ratio ($p = 0.015$) in BC women, also be attributed to the novel functions of enzyme stearoyl-CoA desaturase-1 (SCD1), related to cancer and possibly this enzyme may be overexpressed and highly active in women with BC in population. The SCD1 is a key regulator of lipid FA composition in mammalian cells and also responsible for the conversion of stearic acid to oleic acid. However, novel functions have been proposed to this enzyme like modulation of metabolic and signaling processes related to cell proliferation, survival, and malignant transformation to cancer. Thereby, has been proposed a relationship between SCD1 activity and tumor growth. In several types of cancers, elevated SCD1 expression and activity have been detected (34).

Even in relation to the polymorphism, others studies also found no association between PPARγ polymorphism and the risk of BC in different populations such as: Caucasian women (12); Mexican women (14); women living in Hawaii and California recruited in a Multiethnic Cohort study (13). These reinforce that the results are still inconclusive.

In this study, only age at first full pregnancy was significantly associated with the development BC, whereas BMI, total body fat, physical activity, and age at menarche, at first full pregnancy and of first mammogram associated of BBC. Epidemiological evidences show that there are factors associated with an increased risk of BC, such as gender being a woman is the strongest risk factor for BC, increasing age, younger age at menarche, and family history. Other factors are associated with a decreased risk, such as earlier age at first birth, breastfeeding, parity, and physical activity (35).

CONCLUSION

The findings of the present study strengthen the hypothesis that women with BC and BBD have different sociodemographic, anthropometric, reproductive, gynecological, and lifestyle characteristics. In addition, significant associations between specific breast tissue SFAs, MUFAs, and 18:1 n-9/18:0 ratio were observed and can be supported by a physiological mechanism involving the enzyme SCD1. No association was observed between PPARγ Pro12Ala

Table IV. Adjusted analysis of risk factors associated with breast cancer and benign breast disease

Variables	BC		BBD	
	OR (95% CI)[a]	p*	OR (95% CI)[a]	p*
BMI (kg/m^2)	2.75 (2.32-3.37)	0.888	2.21 (1.96- 2.53)	0.005
Total body fat (%)	2.69 (2.40-3.06)	0.888	3.07 (2.75-3.46)	0.024
Age at menarche (years)	2.34 (1.89 -3.11)	0.273	2.06 (1.77-2.50)	0.008
Age at first full pregnancy (years)	3.14 (2.84 -3.52)	0.004	3.26 (2.97-3.60)	< 0.001
Age of first mammogram (years)	2.66 (2.54 -2.80)	0.467	2.57 (2.46 -2.69)	0.018
Physical activity	1.81 (1.32-3.49)	0.171	1.71 (1.35-2.61)	0.036

*BC: breast cancer; BBD: benign breast disease; BMI: body mass index; CI: confidence interval; OR: odds ratio; *Derived from multiple logistic regression model adjusted for all the above variables.*

polymorphism and the studied groups, which reinforces the need for further studies since the literature shows inconclusive results on this polymorphism and breast cancer.

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