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Trabajo Original

Epidemiología y dietética

Association of coffee intake and its polyphenols with mammographic findings in women who visited the Brazilian Public Health Service

Asociación de la ingesta de café y sus polifenoles con hallazgos mamográficos en mujeres atendidas en el Servicio de Salud Pública de Brasil

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Abstract

Objective: this study aimed to evaluate if there is an association of intake of coffee and its polyphenols with mammographic findings in women treated at a breast care service unit of the Unified Health System (SUS), Brazil.

Research methods and procedures: this was a cross-sectional study with 532 women treated at a health service. The participants were divided according to their mammographic reports into two groups: without and with altered findings. Two 24-h dietary recalls were applied and coffee consumption was categorized into three groups (less than 1 cup, 1 to 3 cups, and more than 3 cups). Phenolic acids were determined using the Phenol Explorer program. The intake of polyphenols was calculated by adding the values obtained from the total amount of coffee consumed during the day. The Multiple Source Method (MSM) was applied to analyze the usual intake.

Results: of the 532 women, 178 (33.5 %) had altered mammographic findings. The participants' average daily coffee intake was 193.4 mL. No significant association was found between coffee consumption and mammographic findings. However, it was found that the second tertile of polyphenols was a protective factor for breast changes.

Conclusion: coffee polyphenols are protective against breast changes in the group evaluated and, thus, can help prevent breast cancer.

Keywords:

Coffee. Polyphenols. Phenolic acids. Mammographic findings. Women.

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Resumen

Objetivo: este estudio tuvo como objetivo evaluar si existe una asociación de la ingesta de café y sus polifenoles con los hallazgos mamográficos de mujeres tratadas en una unidad de patología mamaria del Sistema Unificado de Salud (SUS), Brasil.

Métodos y procedimientos de investigación: este fue un estudio transversal con 532 mujeres tratadas en un servicio de salud. Las participantes se dividieron de acuerdo con sus informes mamográficos en dos grupos: sin y con hallazgos alterados. Se aplicaron dos registros dietéticos de 24 horas y el consumo de café se clasificó en tres grupos (menos de 1 taza, 1 a 3 tazas y más de 3 tazas). Los ácidos fenólicos se determinaron utilizando el programa Phenol Explorer. La ingesta de polifenoles se calculó sumando los valores obtenidos de la cantidad total de café consumido durante el día. Se aplicó el método de fuentes múltiples (MSM) para analizar la ingesta habitual**.**

Resultados: de las 532 mujeres, 178 (33,5 %) tenían hallazgos mamográficos alterados. La ingesta diaria promedio de café de los participantes fue de 193,4 ml. No se encontró una asociación significativa entre el consumo de café y los hallazgos mamográficos. Sin embargo, se encontró que el segundo tercil de polifenoles era un factor protector para los cambios mamarios.

Conclusión: los polifenoles del café son protectores contra los cambios mamarios en el grupo evaluado y, por lo tanto, podrían ayudar a prevenir el cáncer de mama.

Palabras clave:

Café. Polifenoles. Ácidos fenólicos. Hallazgos mamográficos. Mujeres.

INTRODUCTION

Chronic noncommunicable diseases, such as cancer, are serious public health problems and are prevalent worldwide and in Brazil. Diet, nutritional status, and physical activity are indicated as protective or triggering elements of cancer development and progression (1,2).

Nutritional risk factors involved in this process include low consumption of whole grains, vegetables, and fruits; excessive consumption of fast foods, processed foods, and sugary drinks; high consumption of red and processed meats; consumption of alcoholic beverages; and overweight or obesity (3).

A dietary habit as described above can lead to oxidant and proinflammatory properties directly related to carcinogenesis, including in the breast (4-6). On the other hand, a diet rich in phytochemicals can exert antioxidant and anti-inflammatory effects (7). Phytochemicals are bioactive compounds present in foods of plant origin. In the human organism, in addition to the effects mentioned, they can prevent angiogenesis and reduce cell proliferation (8-10).

Coffee is one of the most widely consumed non-alcoholic beverages globally. Brazil is one of the largest coffee consumers in the world, second only to Finland. There are several components present in coffee, such as caffeine, fibers (mainly insoluble fibers, however, with antioxidant capacity due to the presence of polyphenols), and minerals. Brazilian coffee (Arabica) has an average of 0.8 to 1.4 % (2.6 to 8.7 mg/g) of caffeine and 0.59 to 8.74 mg/g of phenolic acids. However, despite the known role of caffeine in health (stimulant of the central nervous system and smooth muscle, in addition to acting on cell differentiation and inhibition of carcinogenesis), studies show that the main benefits of coffee come from phenolic compounds (11-15).

Phenolic acids are phytochemicals belonging to the polyphenol class. Among the acids found in coffee, the notable ones are the hydroxycinnamic acids (caffeoylquinolic acid, feruloylquinolic acid, and caffeic acid), which act as antioxidants, cardioprotectants, and inhibitors of breast cancer tumor cells (16-23).

Many studies investigated the associations of phytochemicals with breast cancer, but few studied their role in mammographic alterations that may or may not become malignant.

Thus, the objective of the present study was to evaluate whether there is an association between coffee polyphenols and mammographic findings in women assisted at a mastology service under the Brazilian Unified Health System (SUS).

MATERIALS AND METHODS

STUDY DESIGN AND SAMPLE

This was a cross-sectional, quantitative and analytical study. The sampling was by convenience and included 532 patients seen at a health service linked to the SUS that specializes in mastology, from April 2015 to February 2017. The individuals included in the research were women aged ≥ 18 years on the date of collection, under the care of the SUS, with mammographic reports, without breast cancer, and without evidence of psychiatric disease that might preclude their participation in the research. All women were included without established inclusion criteria, adopting only pregnancy and lactation exclusion criteria, because under these conditions coffee consumption is often already limited (24).

CLINICAL AND ANTHROPOMETRIC DATA

The *Breast Imaging-Reporting and Data System* (BI-RADS) has been adopted as a model to standardize mammographic findings and was used to assess the participants' mammographic findings to stratify the participants into two groups. Group 1 had altered mammographic findings, which presented as categories 0, 3, 4, and 5 (category 6 was excluded because it was indicative of breast neoplasia). Group 2 exhibited normal mammographic findings, which included categories 1 or 2. Category 0 is considered to be of inconclusive interpretation. Category 1 is considered negative for malignancy and with a 0% risk of breast cancer. Category 2 is considered benign and also has a 0% risk of breast cancer. Category 3 is probably benign and up to a 2% risk of cancer. Category 4 presents a suspicious diagnosis and 2 to 95% of malignancy. Category 5 is considered highly suggestive of malignancy and with a probability greater than 95% risk of cancer. Category 6 is considered a proven malignant lesion. Category 0 was included in Group 1 because the mammographic findings demanded additional tests, and category 3, because the findings could not rule out non-benign alteration (25,27,28).

Each participant's weight was obtained using calibrated anthropometric scales (Filizola®, São Paulo, Brazil) with a capacity of 200 kg. Height was determined using a coupled stadiometer with a capacity of 2 meters (29). The Body Mass Index (BMI) was calculated according to the ratio of weight (BP) to height (H) squared (BMI = BP/A²), and the results were expressed in kilograms per square meter (kg/m²). The BMI classification criteria used were those proposed by the World Health Organization (30) for adults and by PAHO or the elderly (31).

Calculation of coffee intake and its polyphenols

Food intake, including coffee e caloric intake, was collected through two 24-hour recordings (R24h). For the research, two R24h were used, the first collected on the day of the interview and the other by telephone, totaling one on the week and the other on the weekend. In the presence of any intercurrence that prevented the performance of the second 24hR, it was ensured that at least 40 % of the sample had availability of two recalls, so that the habitual consumption of the individual could be estimated (32). The data were analyzed using the Brasil Nutri program, with later inclusion in the Statistical Analysis System (33). The *Multiple Source Method* (MSM) was used in the analysis of usual intake to minimize intrapersonal differences (34).

All participants reported the amount of coffee infusion (mL) consumed, the coffee blend used (Arabic), and if there were additional ingredients, such as milk, sugar, or sweetener. Arabic coffee has a lower amount of caffeine compared to robusta coffee. The protein content in dry grains ranges from 11 to 15 %, lipids from 7 to 16 %, and insoluble fiber is preferable. In relation to chlorine acids, they have an average of 4.5 % after roasting (15).

Coffee consumption was categorized into three groups: less than 1 cup/day, 1 to 3 cups/day, and more than 3 cups/day, with 1 cup corresponding to 50 mL (35). The intake of phenolic acids present in coffee was determined by the Phenol Explorer program (available at www.phenol-explorer.ue) (36). It was calculated by adding the values obtained from each phenolic acid present in the daily amount of coffee ingested. The phenolic acids analyzed in this study were those found in coffee in general: hydroxycinnamic acids (3-caffeoylquinic acids, 4-caffeoylquinic acids, 5-caffeoylquinic acids, 5-feruloylquinic acids and caffeic acid), alkylmethoxyphenols (4-ethylguaiacol and 4-vinylguaiacol), and other polyphenols (catechol, pyrogallol, and phenol) (15,37-39).

STATISTICAL ANALYSIS

The statistical analysis was performed using the SPSS Statistics 20.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to verify the normality of quantitative variables. The chi-squared test was utilized for categorical variables, and Spearman's correlation test was utilized for continuous variables. Analysis of variance, Kruskal-Wallis, Mann-Whitney U, and logistic regression tests adjusted for age, race, income, smoking, caloric intake, physical activity, and BMI were used to determine the association between mammographic findings, phenolic acids, and coffee consumption. In all tests, $p < 0.05$ was considered statistically significant. All variables were collected on the first day of the survey using a structured form.

The present study was approved by the Ethics Committee of the Universidade Estadual do Ceará, under CAAE number: 18054613.0.0000.5534, with Opinion number 314351, and all participants signed a free and informed consent form.

RESULTS

The study comprised women with a mean age of 52.1 ± 9.1 years, most of them married (52.4 %) and with at least an incomplete high school education (52.1 %). Of the 532 women, 178 (33.5 %) presented with altered mammographic findings.

The mean daily coffee intake of the participants was 193.4 mL, and 86.5 % of the women consumed coffee daily. In terms of their BMI, the average value was 28.7 kg/m², and 71.2 % of the women were found to be overweight.

Table I shows the distribution of women according to mammographic findings and demographic, socioeconomic, clinical, and dietary variables, associated with coffee consumption. The variables are: smoke, physical activity, breastfeeding, BMI, age, schooling, race, and family income.

A significant association was found between coffee intake and age group, wherein the higher the coffee consumption, the lower the mean age of the participants ($p = 0.022$).

Table II shows the distribution of polyphenols associated with coffee intake. The average intake of total polyphenols was 375.59 mg/day, divided into: hydroxycinnamic acids (371.5 mg/day), alkylmethoxyphenols (2.12 mg/day), and other polyphenols (2.05 mg/day). A positive association was observed between polyphenols and coffee intake categories, in that the higher the coffee intake, the higher the consumption of phenolic acids and other polyphenols ($p < 0.001$). Moreover, an association between coffee consumption and caloric intake was observed, with a higher caloric intake for those who ingested more than 3 cups of coffee per day ($p = 0.018$).

In logistic regression performed between coffee consumption and mammographic findings according to BI-RADS, no significant association was found, even after adjustment for age, race, income, education attainment level, smoking habit, and BMI stratification. There was also no statistically significant trend that evidenced increased consumption of polyphenols reducing the risk for breast changes.

However, when the coffee components were analyzed in their tertiles, the second tertile of polyphenols was found to be a protective factor for breast alterations (Table III).

Table I. Distribution of the women evaluated according to risk variables for breast cancer and coffee consumption categories. Fortaleza, Brazil, 2020

Variables	Coffee consumption, cups/day*			p†
	< 1 (n = 44)	1-3 (n = 69)	≥ 3 (n = 419)	
Clinical variables				
Mammographic findings, altered‡	14 (31.8)	18 (26.1)	146 (34.8)	0.350
Smoke, yes‡	7 (15.9)	6 (8.7)	36 (8.6)	0.278
Practice of physical activity, no	33 (75.0)	50 (72.4)	320 (76.4)	0.805
Breastfeeding, no	30 (68.2)	36 (52.2)	246 (58.7)	0.599
BMI, overweight‡	30 (75.0)	47 (70.1)	303 (74.9)	0.704
Socioeconomic variables				
Age, years‖	54,5 (9.7)	54.0 (9.7)	51,5 (8.9)	0.022
Schooling, ≤ 8 years‡	21 (47.7)	36 (52.2)	194 (46.3)	0.934
Race, not Caucasian‡	41 (93.2)	56 (81.1)	325 (77.6)	0.089
Family income, < 1 SM‡,§	34 (85.0)	54 (80.6)	330 (81.7)	0.842

**Cup equivalent to 50 mL; †Kruskal-Wallis test; ‡Values expressed as n (%); §n = 511; ‖Values expressed as mean (dp).*

Table II. Distribution of women assessed according to caloric intake, classes and subclasses of coffee polyphenols, and coffee consumption categories. Fortaleza, Brazil, 2020

Variables	Coffee consumption, cups/day*			p†
	< 1 (n = 44)	1-3 (n = 69)	≥ 3 (n = 419)	
Energy, kcal‡	1563.2 (1282.5-1781.1)	1492.5 (1297.9-1735.0)	1622.6 (1382.1-1852.7)	*0.018*
Phenolic acids, mg‡	0.00 (0.0-0.0)	194.2 (145.6-194.2)	412.8 (388.5-582.7)	*< 0.001*
Hydroxycinnamic acids, mg‡	0.00 (0.0-0.0)	193.2 (144.7-193.2)	410.4 (386.2-579.5)	*< 0.001*
3-Caffeoylquinic acids,mg‡	0.00 (0.0-0.0)	57.5 (57.5-68.3)	111.7 (92.9-136.3)	*< 0.001*
4-Caffeoylquinic acids, mg‡	0.00 (0.0-0.0)	66.2 (66.2-78.6)	128.5 (107.0-156.9)	*< 0.001*
5-Caffeoylquinic acids, mg‡	0.00 (0.0-0.0)	77.8 (77.8-92.3)	151.0 (125.7-184.3)	*< 0.001*
5-Feruloylquinic acid, mg‡	0.00 (0.0-0.0)	12.9 (12.9-15.4)	25.2 (20.9-30.7)	*< 0.001*
Caffeic acid, mg‡	0.00 (0.0-0.0)	0.036 (0.03-0.04)	0.07 (0.05-0.08)	*< 0.001*
Alkylmethoxyphenols, mg‡	0.00 (0.0-0.0)	1.1 (0.82-1.1)	2.33 (2.2-3.3)	*< 0.001*
4-Ethylguaiacol, mg‡	0.00 (0.0-0.0)	0.71 (0.7-0.8)	1.38 (1.1-1.6)	*< 0.001*
4-Vinylguaiacol, mg‡	0.00 (0.0-0.0)	0.51 (0.51-0.6)	0.99 (0.82-1.2)	*< 0.001*
Other polyphenols, mg‡	0.00 (0.0-0.0)	1.06 (0.79-1.06)	2.26 (2.13-3.19)	*< 0.001*
Phenol, mg‡	0.00 (0.0-0.0)	0.45 (0.4-0.5)	0.87 (0.7-1.06)	*< 0.001*
Catechol, mg‡	0.00 (0.0-0.0)	0.13 (0.13-0.15)	0.25 (0.2-0.3)	*< 0.001*
Pyrogallol, mg‡	0.00 (0.0-0.0)	0.60 (0.6-0.7)	1.16 (0.9-1.4)	*< 0.001*
Total polyphenols, mg‡	0.00 (0.0-0.0)	195.3 (146.5-195.3)	415.0 (390.6-585.9)	*< 0.001*

**Cup equivalent to 50 mL; †Kruskal-Wallis test; ‡Values expressed as median (p25-p75).*

Table III. Odds ratio (OR) and confidence interval (CI) corresponding to coffee consumption and polyphenol tertiles in relation to mammographic findings in women. Fortaleza, Brazil, 2020

	OR (95 % CI)	
	Model 1	**Model 2**
Coffee consumption		
< 1	Reference	Reference
1-3	0.69 (0.29-1.64)	0.37 (0.10-1.29)
≥ 3	1.03 (0.52-2.06)	0.67 (0.27-1.66)
p-trend*	0.504	0.835
Total polyphenols		
1 tertile	Reference	Reference
2 tertile	*0.61 (0.38-0.96)*	0.73 (0.38-1.40)
3 tertile	0.97 (0.60-1.56)	0.52 (0.24-1.13)
p-trend*	0.938	0.098

1 x cup/day. Model 1: altered mammographic findings (BI-RADS 0, 3, 4, and 5). Model 2: altered mammographic findings (BI-RADS 3, 4, and 5). Variables adjusted for age, race, income, smoking, caloric intake, physical activity, and BMI. Test performed: logistic regression (trend test).

DISCUSSION

The participants' mean coffee and mean coffee polyphenol intake were 193.4 mL/day and 375.59 mg/day, respectively. A study conducted with the Japanese population found that the average amount of coffee consumed was 426 mg/day, and that polyphenols from coffee accounted for 50 % of total consumption of polyphenols in the Japanese diet. In a study published by the same author in 2020, consumption of coffee polyphenols was 655 mg/day, which amounted to 53 % of total consumption of polyphenols in the Japanese diet (40-42).

On the other hand, a study conducted with 557 Brazilians found that the average coffee consumption of Brazilians was 143.4 mL/day, and the average consumption of polyphenols from coffee, 247 mg/day (35). In a study conducted in Fortaleza with 498 college students, the average coffee consumption was 199 mL/day, much closer to that found in this study (43).

Coffee is one of the most consumed beverages in the world and has several health benefits, including a high level of antioxidant activity (44,45).

In the present study, the group of women with lower coffee consumption (less than 1 cup/day) showed a higher percentage of participants with breast changes, according to the BI-RADS; however, this association did not present a statistical significance (p = 0.345). However, when the coffee components were analyzed, the second tertile of coffee polyphenols was found to be protective against breast changes (CI: 0.38-0.96).

Studies show that one effect of polyphenols, specifically phenolic acids, is the neutralization of the free radicals produced by the body that are associated with chronic diseases, such as cancer and cardiovascular diseases. Thus, polyphenols can act preventively in breast cancer by acting on breast changes, even without cell malignancy (46-48).

This is the first study to focus on the association of the consumption of coffee and its polyphenols with mammographic findings, though there have been several previous studies that show the relationship between coffee consumption and a lower risk of breast cancer (49,50). In a study by Lowcock and colleagues (2013), a significant 29 % reduction in the risk of breast cancer was found in those who consumed more than 5 cups/day of coffee. A meta-analysis published in 2013 showed an inverse association between coffee consumption and the risk of breast cancer, even in those with a mutation in the BRCA1 gene (51).

Another benefit attributed to coffee is related to caffeine. It is involved in the metabolism and is one of the best markers of human cytochrome P450 1A2, which is involved in estrogen metabolism and thus has a key role in breast cancer etiology (52,53). However, despite the several benefits of caffeine, studies show that even decaffeinated coffees can aid in the prevention of several chronic diseases due to being rich in polyphenols (54-56). These phytochemicals inhibit the oxidation process, in addition to acting as detoxifiers and repairers. One of the mechanisms involved in this process is the activation of the NF-E2-related factor 2 system that induces the expression of cell defense genes (44,45,57).

A study conducted in Spain with 10,812 women found no association between coffee consumption and the overall risk of breast cancer. However, it was also found that postmenopausal women who consumed more than 1 cup of coffee/day had a lower risk of the disease (58).

In the same study, it was found that those with greater coffee consumption (more than 1 cup/day) had a higher mean age (35.9 years) (58). Conversely, in the present study, the mean age was lower (51.5 years) for those with greater coffee consumption (more than 3 cups/day). In a study conducted with the elderly that evaluated the relationship between coffee and longevity, a lower mean age was found in those with higher coffee consumption (more than 4 cups/day) (59).

The data from our study coincided with the findings of a study conducted in Brazil (ELSA-Brazil). ELSA is a cohort study conducted in six Brazilian cities with 4,426 participants, and one of the objectives was to verify the association of coffee consumption with clinical and demographic variables related to the risk of cardiovascular disease. The authors found a significant association between coffee consumption and mean age, with a lower mean age (49 years) of individuals with greater coffee consumption (more than 3 cups/day). Thus, it can be concluded that young adult women have the greatest coffee intake (60). In a study by Camargo et al. (61), it was also detected that there was a progressive increase in coffee consumption in the 30-39 age group and a decline in the elderly.

In the study by Miranda et al. (60), a higher caloric intake was found in individuals who consumed more coffee (more than 3 cups/day), which is similar to this study's findings. This association of coffee consumption with caloric intake was also verified in another study, which evaluated the association between coffee intake and the risk of hypertension (62). One of the hypotheses attributing to this is that coffee consumption is often accompanied by snacks and more caloric foods, such as bread, cookies, and pasta. Sugar, which is often used to sweeten coffee, also contributes to the increase in daily caloric intake. This association between coffee consumption and caloric intake may also contribute to the association of coffee polyphenols with breast changes (63).

In the present study, it was not verified whether the intake of coffee was accompanied by foods of higher energy density, which can be cited as one of its limitations; like this the consumption of antioxidants from other sources was not collected.

The findings of this study indicate that coffee consumption can be recommended in addition to a healthy diet as a strategy for the prevention of chronic diseases.

CONCLUSIONS

Coffee polyphenols (second tertile) were protective against breast alterations in the evaluated group and may help in the prevention of breast cancer.

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