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ORIGINAL PAPER

Consumption of processed and ultra-processed foods by patients with stomach adenocarcinoma: a multicentric case–control study in the Amazon and southeast regions of Brazil

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Abstract

Purpose There is limited information about the dietary habits associated with stomach adenocarcinoma in the Brazilian population, so our purpose is to analyze the consumption of processed and ultra-processed foods by patients with stomach adenocarcinoma in Brazil.

Methods A multicentric hospital-based case–control study was conducted in São Paulo (southeastern region) and Belém (Amazon region) of Brazil with 1,045 individuals, both sexes, between 18 and 75 years old. In São Paulo, there were 214 cases with stomach adenocarcinoma and 150 controls patients submitted to stomach endoscopy named as Group I (without any pre-malignant gastric disease) and the Healthy Controls (Group 2) comprised 401 individuals matched by age and sex from the prevention unit at A.C .Camargo Cancer Center. In Belém, it has two groups one are cases 140 and second 140 hospital controls, recruited in outpatient clinics. Lifestyle and food frequency questionnaires (FFQ) were administered in cases and controls in both places. Univariate and multivariable binomial logistic regression analyses were performed.

Results In São Paulo, cases reported two times greater consumption of processed meat (adjusted OR 2.56, 95% CI 1.32–4.96) and of sweets (≥ 80 g/day) than Group 1 (endoscopic controls) (adjusted OR 2.25, 95% CI 1.21–4.18). Compared with Group 2, processed food consumption (≥ 44 g/day) as well as ≥ 44 g/day of salted bread increased the odds of having stomach adenocarcinoma (adjusted OR 2.96, 95% CI 1.82–4.81 and adjusted OR 2.03, 95% CI 1.30–3.18), respectively. In Belém, individuals who reported consuming ≥ 166 g/day of fried and roasted meat and fish were more likely to have stomach adenocarcinoma (adjusted OR 2.21, 95% CI 1.13–4.30).

Conclusions In both cities, consumption of processed and ultra-processed foods, especially salted bread, yellow cheese, fried and roasted meats, fish fried, processed meat, and sweets, was independently associated with the chance of having stomach adenocarcinoma.

Keywords Stomach cancer · Diet · Lifestyle · Case–control study · Brazil

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Introduction

Stomach cancer is the fifth most common type of cancer in the world and the fourth leading cause of cancer-related death [1]. In Brazil, the estimated number of new stomach cancer cases for each year of the triennium 2020–2022 is 21,230, with age-standardized incidence rates of 12.8/100,000 for men and 7.3/100,000 for women [1, 2]. Although the stomach cancer mortality rate in Brazil decreased from 1996 to 2012, it remains high and differs among geographic regions of the country. The incidence rate has followed the global decreasing trend in São Paulo, whereas, in Belém, it was stable in men and increased in women in the period 1996–2010 [3–6].

Various risk factors, including *Helicobacter pylori* infection and Epstein–Barr virus positivity, have been associated with the presence of stomach adenocarcinoma. Food habits such as high consumption of salt and ultra-processed foods, consumption of > 35–40 g/day alcohol, and low fruit and vegetable intake have also been identified as risk factors, while high consumption of fruit has been shown to reduce this risk [7].

Food habits changed between 1987 and 2009 throughout the world, including in Brazil, with fresh and minimally processed foods of vegetable origin (e.g., rice, beans, cassava, potatoes, and vegetables) being replaced by industrialized (processed and ultra-processed) ready-to-eat products, leading to excessive daily calorie intake [8]. Monteiro et al. [9] described an increase in the consumption of ultra-processed foods from outside the home, which contributed to chronic disease development, in the Brazilian population. The NOVA food classification system has identified increasing trends in the production and consumption of ultra-processed food and drink products throughout the world [10].

At present, there is limited information about the association of food habits with the development of stomach adenocarcinoma in the Brazilian population. The objective of this case–control study was to analyze the consumption of processed and ultra-processed food in patients with stomach adenocarcinoma, in two cities in the southeast and Amazon regions of Brazil.

Methods

Study population

This study was part of a hospital-based multicentric case–control study on stomach adenocarcinoma "Genomics and epidemiology for gastric adenocarcinomas in Brazil" (FAPESP grant no. 2014/26897–0) conducted at the A.C.Camargo Cancer Center, São Paulo (southeast region of Brazil), and the Hospital Ophir Loyola and General Hospital Universitário João de Barros Barreto, Belém (Amazon region of Brazil). Recruitment was conducted from April 2016 to February 2019 in São Paulo and from July 2017 to April 2019 in Belém.

The study was approved by the Committee on Ethics in Human Research of the Antônio Prudente Foundation Cancer Hospital of A. C. Camargo Cancer Center (no. 1.480.537), and the Hospital Ophir Loyola and General Hospital Universitário João de Barros Barreto (no. 2.395.946). All participants provided written informed consent.

The sample size calculation used a study power (1 – β) of 80%, alpha error rate of 5%, and odds ratio (OR) of 2 for a two-tailed hypothesis and indicated that a minimum of 133 cases and 133 controls were needed. The cases were patients who were treated at the participating centers with histologically confirmed stomach adenocarcinoma, classified according to the *International Classification of Diseases for Oncology*, third edition (ICD-O3). In São Paulo, the controls were recruited in two groups at the A.C.Camargo Cancer Center, as follows: Group 1 was comprised of patients with negative results for malignancy and preneoplastic lesions, who underwent upper-digestive endoscopy; Group 2 was composed of asymptomatic individuals participating in a cancer prevention campaign. In Belém, the control group were individuals recruited in outpatient clinics (physiotherapy, dentistry, nutrition, and psychology) of the Hospital Universitário João de Barros Barreto. The difference of recruitment between control groups was because in São Paulo there was a prevention clinic where healthy controls (Group 2) were recruited. While in Belém, the controls were hospitals from clinics where patients had no diagnosis of gastric cancer and no clinical suspicion. Cases and controls were matched by frequency according to sex and age (18–75 years, in 5-year groups). All controls were interviewed in the same period of case recruitment.

The exclusion criteria for participation in the study were previous malignancy except non-melanoma skin cancer, preneoplastic lesions (such as intestinal metaplasia), and no physical conditions such as patients with impaired mobility due to illness, or mental and cognition condition precluding to understand the questions made by the interviewers.

Procedures and instruments

Nutritionists trained for interview administered questionnaires and conducted face-to-face interviews with the study participants.

A sociodemographic questionnaire was used to collect information on participants' sex, age, marital status, education level, and skin color. The lifestyle factors evaluated were

alcohol and tobacco consumption and weight status that was available in the medical record. Participants were classified according to their body mass index (BMI) as underweight, eutrophic, overweight, and obese [11]. A Food Frequency Questionnaire (FFQ) validated for the Brazilian population with cancer [12] was adapted with inclusion regional Belém foods. For each food, the participants indicated the frequency, the number of times consumed (1–10) per day, week, month, or year. The size of the ingested portion was presented as small, medium, or large represented in slices, spoons, and transformed into grams according to each type of food. The consumption (grams/day) was calculated as follows: ((frequency × portion)/days)) × grams (e.g., 2 portions of 50 g of bread, consumed 7 times/week). The consumption values, foods, and food groups were stratified into terciles.

The food consumption was presented for each participant at the centers. For the assessment, the foods consumed were classified as processed or ultra-processed (Table 1). Processed foods included culinary or by industrial products group prepared food for meals served in homes and restaurants, and ultra-processed foods group included formulated foods to reduce microbial deterioration ("long shelf life"), which are mostly highly palatable and easy to prepare and/or consume [10].

Some food groups described in Table 1 had low consumption and, to enable the analysis, the following were grouped: (1) Sweets in general (Cakes with or without filling, whipped cream, confectionery sweets/ Cookies with or without filling/ Made sweets (cornflakes, chocolate, gelatin, candies, chocolates, ice cream)); (2) Pizza, fried, and baked snacks/ Popcorn and snacks; and (3) Seasonings (salt, soy sauce, mayonnaise for sauce, and vinaigrette)/ Other industrialized spices (ketchup / mustard and industrialized pepper sauce).

Statistical analyses

The chi-squared test was used to examine differences in demographic and lifestyle characteristics between cases and controls. Univariate and multivariable binomial regression analyses with logistic link function were performed separately for each region to obtain the exponential β to identify the odds ratios (OR) with 95% confidence intervals (CIs) for the outcome of stomach adenocarcinoma. The multiple regression models were adjusted using the Hosmer–Lemeshow test which was built with the following assumptions: improvement in accuracy, as reflected by 95% CIs which measure the stability of OR and total degrees of freedom allowed for each outcome variable (overfitting control) [13, 14]. The Wald test was calculated to determine statistical significance.

> "The multiple regression models were adjusted for confounding variables tobacco and alcohol consumption, BMI, and social variables, education level and marital status."

The data were entered into the Research Electronic Data Capture (REDcap) platform (Vanderbilt University, Tennessee, USA) and statistical analyses were performed using the Statistical Package for Social Science SPSS (version 23.0 for Windows).

Table 1 Classification of processed and ultra-processed food consumption in a multicentric case–control study, in São Paulo (southeast region) and Belém (Amazon region), Brazil

Processed	Ultra-processed
Salted bread	Sugary drinks (industrialized juice and soft drinks)
Brown rice	Cakes with or without filling, whipped cream, confectionery sweets
Refined/white rice	Cookies with or without filling
Yellow cheeses (plate, mozzarella)	Made sweets (cornflakes, chocolate, gelatin, candies, chocolates, ice cream)
Whole grain bread	Other industrialized spices (ketchup/mustard and industrialized pepper sauce)
Leguminous (beans and lentils)	Industrial soup and noodles
Pasta (lasagna noodles with or without meat)	Processed meat, sausage, cold cuts and "*tropeiro* beans" (sausage, bacon, canned and dried meat, and nuggets)
Seasonings (salt, soy sauce, mayonnaise for sauce and vinaigrette)	Pizza, fried and baked snacks
French fries	Popcorn and snacks
Meat and fish (*Pirarucu*, salted fish*) (processed with culinary ingredients and fried or baked)	

Classification, according to Monteiro et al. [10]. Ultra-processed foods include foods formulated to reduce microbial deterioration (i.e., increase shelf life), which tend to be highly palatable and easy to prepare and/or consume

*Consumed in the Amazon region of Brazil

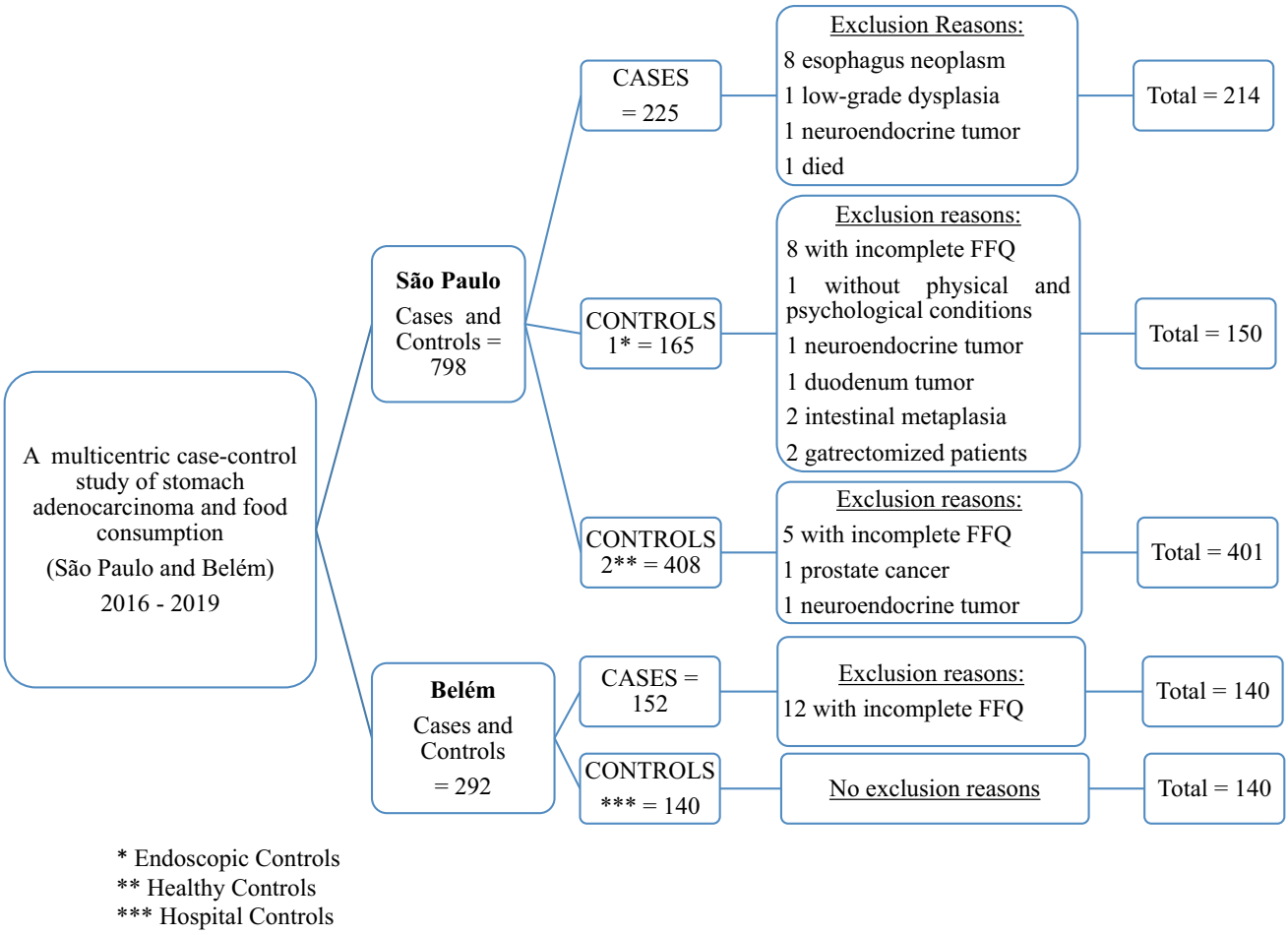

Fig. 1 Flow chart of participant selection

Results

This multicentric case–control study consisted of 214 and 140 cases with stomach adenocarcinoma in São Paulo and Belém, respectively, while there were 150 controls in Group 1 (upper-digestive endoscopy) and 401 controls in Group 2 (healthy controls) in São Paulo, and 140 hospital controls in Belém (Fig. 1).

The majority of cases occurred in males aged > 60 years in São Paulo and Belém. In São Paulo, about 17.5% of the cases were smokers, 42% were ex-smokers, and 48.6% consumed alcohol. In Belém, low weight was observed in 36.7% ($n = 51$) of the cases, 65.7% ($n = 92$) were ex-smokers, and 60.7% ($n = 85$) consumed alcohol (Table 2).

In São Paulo, between cases and endoscopic controls, significant differences were observed for education level, BMI, tobacco consumption, and number of cigarettes smoked/day, while between cases and healthy controls there were differences for skin color, education level, BMI, tobacco consumption, the number of cigarettes smoked/day, and alcohol consumption. In Belém, between cases and controls, differences were observed for skin color, education level, BMI, and tobacco and alcohol consumption (Table 2).

Univariate regression analysis was performed to identify the OR, according to foods or groups (Supplementary Tables S1 and S2). In São Paulo, when comparing cases versus endoscopic controls, it was observed that patients with salted bread consumption between 16 – 43 g/day and ≥ 44 g/day had a chance to present stomach adenocarcinoma ($OR = 2.70$, 95% CI 1.30 – 5.59 and $OR = 1.66$, 95% CI 1.02 – 2.73, respectively) when comparing cases and healthy controls who had consumption between 16 – 43 g/day and ≥ 44 g/day of bread were more likely to have stomach adenocarcinoma ($OR = 1.82$, 95% CI 1.08 – 3.08) and $OR = 2.45$, 95% CI 1.63 – 3.67, respectively).

Endoscopic controls with white rice consumption ≥ 125 g/day were twice as likely to have stomach adenocarcinoma ($OR = 2.23$, 95% CI 1.01–4.93). Endoscopic and healthy control groups had an increased chance of having stomach adenocarcinoma when leguminous consumption was ≥ 102 g/day ($OR = 2.30$, 95% CI 1.35–3.94 and $OR = 1.55$, 95% CI

Table 2 Sociodemographic characteristics of cases and controls in São Paulo (southeast region) and Belém (Amazon region), Brazil, 2016–2019

Variables	São Paulo						Belém			
	Cases (214)		Controls 1 (150)		Controls 2 (401)		Cases (140)		Controls (140)	
	N	%	N	%	N	%	N	%	N	%
Sex										
Male	135	63.1	80	53.3	235	58.6	86	61.4	86	61.4
Female	79	36.9	70	46.7	166	41.4	54	38.6	54	38.6
Age										
≤45	36	16.8	32	21.3	66	16.5	30	21.4	30	21.4
>45 to 60	80	37.4	60	40.0	165	41.1	53	37.9	56	40
≥61	98	45.8	58	38.7	170	42.4	57	40.7	54	38.6
Skin color										
White	138	64.5	101	67.8	191	47.8‡	13	9.3	29	20.7‡
Black	13	6.1	4	2.7	59	14.8	9	6.4	25	17.9
Pardo	42	19.6	29	19.5	91	22.8	118	84.3	86	61.4
Others	21	9.8	15	10.1	59	14.8				
Schooling*										
Illiterate/<5 years	33	15.4	9	6.1∞	42	11.3‡	66	47.1	23	16.4‡
6 to 12 years	35	16.3	25	16.8	80	20.1	43	30.7	42	30.0
High school	65	30.4	48	32.2	155	38.8	26	18.6	46	32.9
Graduation	56	26.2	58	38.9	106	26.5	5	3.6	24	17.1
Postgraduate	25	11.7	9	6.0	14	3.5	0	0	5	3.6
Marital status*										
Single	23	10.7	19	12.7	51	12.8	31	22.1	30	21.4
Married	168	78.5	104	69.3	295	73.8	90	64.3	87	62.1
Widower	11	5.1	14	9.3	19	4.8	7	5	13	9.3
Divorced	12	5.6	13	8.7	35	8.8	12	8.6	10	7.1
BMI (kg/m^2)*										
Low weight	40	18.8	3	2.0‡	41	10.3∞	51	36.7	24	17.1‡
Eutrophic	81	38.0	62	41.6	142	35.6	64	46	74	52.9
Overweight	52	24.4	53	35.6	123	30.8	13	9.4	36	25.7
Obese	40	18.8	31	20.8	93	23.3	11	7.9	6	4.3
Smoking*										
No smoker	86	40.6	87	59.2‡	238	59.8‡	47	33.6	86	58.6‡
Ex-smoker	89	42.0	52	35.4	129	32.4	92	65.7	40	28.6
Smoker	37	17.5	8	5.4	31	7.8	1	0.7	18	12.9
Number of cigarettes smoked/day										
≤20	97	77.6	50	83.3‡	139	86.9∞	76	82.6	49	84.5
>20	28	22.4	10	16.7	21	13.1	16	17.4	9	15.5
Alcohol consumption*										
No	109	51.4	71	48.3	277	69.6‡	55	39.3	102	72.9‡
Yes	103	48.6	76	51.7	121	30.4	85	60.7	38	27.1
Alcohol consumed*										
<12 g/day	158	74.5	118	80.3	326	81.9∞	60	42.9	102	72.9‡
12–47 g/day	37	17.5	23	15.6	39	9.8	16	11.4	10	7.1
>47 g/day	17	8.0	6	4.1	33	8.3	64	45.7	28	20

Controls 1 = endoscopic controls (Group 1); Controls 2 = healthy controls (Group 2); controls from Belém = hospital controls; ∞$p<0.05$ and ‡$p<0.001$; *missing values: education, $n=1$ register for São Paulo cases and controls 1); marital status, $n=1$ register for São Paulo controls 2; BMI, $n=1$ register for São Paulo cases and controls 1 and Belém cases, $n=2$ registers for São Paulo controls 2; and smoking, alcoholism, and the amount of alcohol consumed, $n=2$ registers for São Paulo cases, $n=3$ registers for São Paulo controls 1 and 2

1.02–2.34, respectively). Likewise, processed meat, sausage, cold cuts and "*tropeiro* beans" (sausage, bacon, canned and dried meat, and nuggets) consumption was associated with stomach adenocarcinoma for both control groups, with a two to three times increased chance of having stomach adenocarcinoma. Pizza, fried and baked snacks, popcorn, and snack consumption ≥ 37 g/day was associated with stomach cancer in healthy controls (*OR* = 1.91, CI 95% 1.27–2.87). In relation to sugar drinks and sweets in general, individuals who had consumption in the last tercile a higher chance of stomach adenocarcinoma (Supplementary Table S1).

Whole grain bread consumption ≥ 6.7 g/day was a protective factor of stomach adenocarcinoma for endoscopic (*OR* = 0.48, 95% CI 0.30–0.76) and healthy controls (*OR* = 0.62, 95% CI 0.43–0.90). Pasta consumption was also a protective factor healthy controls (*OR* = 0.53, 95% CI 0.35–0.80) (Supplementary Table S1).

In Belém, salted bread consumption was a risk factor of stomach adenocarcinoma when intake was 49–100 g/day (*OR* = 3.31, 95% CI 1.78–6.17) and ≥ 101 g/day (*OR* = 4.44, 95% CI 2.33–8.47). Individuals who consumed fried and roasted meat ≥ 166 g/day showed a chance of 2.45 (95% CI 1.36–4.42), while sugary drink consumption between 9 and 76.5 g/day increased the chance almost three times (*OR* = 2.75, 95% CI 1.50–5.06) and ≥ 76.6 g/day increased the chance of stomach adenocarcinoma by about five times (*OR* = 4.73, 95% CI 2.51–8.89) (Supplementary Table S2).

In Belém, it was observed that yellow cheese consumption ≥ 8.7 g/day showed an 84% decreased chance of stomach cancer (*OR* = 0.16, 95% CI 0.08–0.29), also individuals who consumed > 1.7 g/day whole grain bread were less likely to have stomach cancer (*OR* = 0.08, 95% CI 0.02–0.36). Similarly, pasta consumption ≥ 54 g/day showed a decreased chance of stomach cancer (*OR* = 0.48, 95% CI 0.02–0.36). In addition, French fries were protective factors (> 5 g/day, OR = 0.29, 95% CI 0.17–0.50), as well as 8.3–32.6 g/day (*OR* = 0.28, 95% CI 0.15–0.52) and ≥ 32.7 g/day (*OR* = 0.25, 95% CI 0.14–0.47) sweets consumption (Supplementary Table S2).

Total consumption of processed and ultra-processed food ≥ 1448 g/day increased the chance of having stomach adenocarcinoma greater than two times in São Paulo and six times in Belém when processed and ultra-processed food were consumed ≥ 913 g/day (Supplementary Tables S1 and S2).

For the cases as compared with the endoscopic controls from São Paulo, the chance of having stomach adenocarcinoma was increased by the consumption of processed meat, sausage, cold cuts, and "*tropeiro* beans" (sausage, bacon, canned and dried meat, and nuggets) between 17 and 43 g/day (adjustedOR 1.89, 95% CI 1.01–3.53) and ≥ 44 g/day (adjustedOR 2.56, 95% CI 1.32–4.96), as well as ≥ 80 g/day sweets in general (adjustedOR 2.25, 95% CI 1.21–4.18) (Table 3).

Regarding cases compared to healthy controls in São Paulo, it was observed an increased chance by the consumption of processed meat, sausage, cold cuts, and "*tropeiro* beans" (sausage, bacon, canned and dried meat, and

Table 3 Multiple regression analysis, adjusted odds ratio, in cases versus controls, for processed food consumption and stomach adenocarcinoma in São Paulo (southeast region), Brazil, 2016–2019

Food	Consumption g/day	Cases versus Endoscopic Controls* adjusted OR (95% CI)	Cases versus Healthy Controls** adjusted OR (95% CI)
Salted bread	≤ 16.5		Ref
	16.6–43		1.57 (0.89–2.79)
	≥ 44		2.03 (1.30–3.18)
Yellow cheeses (plate, mozzarella)	≤ 2.6	Ref	
	2.7–9.9	1.92 (0.98–3.77)	
	≥ 10	0.88 (0.46–1.67)	
Sweets in general (Cakes with or without filling, whipped cream, confectionery sweets/ Cookies with or without filling/ Made sweets [cornflakes, chocolate, gelatin, candies, chocolates, ice cream])	≤ 33.2	Ref	
	33–79	1.74 (0.91–3.32)	
	≥ 80	2.25 (1.21–4.18)	
Processed meat, sausage, cold cuts and "*tropeiro* beans" (Sausages and others (sausage, bacon, canned and dried meat, and nuggets)	≤ 16	Ref	Ref
	17–43	1.89 (1.01–3.53)	1.98 (1.24–3.18)
	≥ 44	2.56 (1.32–4.96)	2.96 (1.82–4.81)

Models adjusted for confounding variables (tobacco and alcohol consumption, BMI), education level, and marital status

*Hosmer–Lemeshow test = 0.613

**Hosmer–Lemeshow test = 0.962

Case (*n* = 212) versus endoscopic control (*n* = 147); Case (*n* = 212) versus healthy controls (n = 397)

nuggets) between 17 and 43 g/day (adjustedOR 1.98, 95% CI 1.24–3.18) and ≥ 44 g/day (adjustedOR 2.96, 95% CI 1.82–4.81), as well as of salted bread consumption ≥ 44 g/day (adjustedOR 2.03, 95% CI 1.30–3.18) (Table 3). In Belém, consumption of ≥ 166 g/day fried and roasted meats and fried fish increased the chance of having stomach adenocarcinoma (adjustedOR 2.21, 95% CI 1.13–4.30) (Table 4).

Discussion

We observed that the consumption of processed and ultra-processed foods, mainly salted bread, yellow cheese, processed meat, and sweets increased the chance of having stomach adenocarcinoma in São Paulo and Belém (Brazil). These types of food may contribute to cancer development due to their higher total and saturated fat, as well as added sugar and salt contents, along with lower fiber and vitamin density and low protein [15–21]. Fiolet et al. [22] reported that ultra-processed food consumption was associated with a 10% increase in general cancer risk.

Monteiro et al. [23] described, in Brazil, an increase in the consumption of ultra-processed foods, which may have contributed to the increased incidence of chronic diseases. Costa Louzada et al. [24] reported that the Brazilian diet had been changing, with traditional meals based on natural or minimally processed foods being replaced with ultra-processed foods. The consumption of added sugar and meat has been shown to be high in Brazil [25, 26]. In São Paulo, sugar consumption increased from 100 to 113 g/day between 2003 and 2008. In addition, the red meat and processed meat intakes were 138 g/day for men and 81 g/day for women, and about 81% of men and 58% of women consumed more meat than recommended [27].

According to the 2018 World Cancer Research Fund report [7], there is sufficient evidence to support that foods preserved in salt contribute to the development of stomach adenocarcinoma; evidence for the contributions of sausages and potatoes remains limited [28, 29]. In these results, patients with stomach adenocarcinoma were characterized by high consumption of ultra-processed foods, increasing the chance of stomach adenocarcinoma by more than two times.

A previous study conducted in São Paulo showed that healthy dietary habits were more frequent among older adults than young adults (36.9% versus 15.4%), and that the Revised Brazilian Healthy Eating Index (BHEI-R) scores improved gradually, and most markedly among older adults, over a 12-year period [30]. The overall population showed increases in total fruit, whole fruit, whole grain, oil, and sodium intakes. The main contributor to socioeconomic inequality in diet quality shifted from ethnicity in 2003 to per-capita household income in 2008 and 2015; age was a persistent factor related to inequality. Concentration indices indicated that individuals with lower incomes had higher BHEI-R scores in 2003, a shift in favor of individuals with higher incomes was noted in 2008 and 2015 [30].

Regarding stomach adenocarcinoma, evidence that the consumption of citrus fruits reduces the risk of gastric cardia adenocarcinoma is also limited [7]. In Brazil, the attributable dietary fractions of low vegetable consumption, low fruit consumption, > 10 g/day salt intake, processed meat consumption, and > 70 g/day red meat intake were 24% for non-cardia stomach cancer and 55% for cardia cancer in women; these percentages were 20% and 55%, respectively, in men [31]. These findings confirm the importance of healthy diets for reducing the risk of stomach adenocarcinoma.

In Belém, higher consumption of salty foods (e.g., jerky, canned meat, shrimp, and salted fish) and carbohydrate-rich foods such as manioc and its derivatives (e.g., flour and *tucupi*) were identified. According to Baiao et al. [32], processing to produce cassava flour can affect the nutritional value of cassava root through molecular changes and nutrient loss. In addition, cassava flour often contains added aniline-based dyes, which are sources of NH_2 and NO_2 radicals, and thus, could act as substrates for the endogenous formation of nitrosamines, which are carcinogens associated with the pathogenesis of stomach adenocarcinoma [33]. Family budget surveys conducted in 2002–2003, 2008–2009, and 2017–2018 have documented reductions in the ingestion of fresh or minimally processed

Table 4 Multiple regression analysis, adjusted odds ratio, in cases versus controls, for processed food consumption and stomach adenocarcinoma in Belém (Amazon Region), Brazil, 2016–2019

Food	Consumption g/day	Cases versus Controls* adjusted OR (95% CI)
Fried and roasted meats (including roasted and fried fish (*Pirarucu*, salted fish—processed with culinary ingredients and fried or roasted)	≤ 106	Ref
	107–165	0.93 (0.48–1.80)
	≥ 166	2.21 (1.13–4.30)

Models adjusted for confounding variables (tobacco and alcohol consumption, BMI), education level, and marital status

*Hosmer–Lemeshow test = 0.966

cases ($n = 139$) versus controls ($n = 140$)

foods and processed culinary ingredients, as well as increases in the intake of processed and ultra-processed foods, in all Brazilian regions, including the Amazon [34].

After adjusted for multiple regression models, our results corroborate that consumption of processed and ultra-processed foods such as meat, sausage, fried and roasted meat, and fried fish is associated with stomach adenocarcinoma in São Paulo and Belém. Meta-analysis studies have shown that the consumption of processed foods, such as processed meat and salt-preserved foods, was associated with the risk of stomach cancer development [35–40].

The associations observed in this study are according to the literature. The consumption of red meat, in which cooking at high temperatures results in the formation of heterocyclic amines and polycyclic aromatic hydrocarbons, has mutagenic potential and has been associated with the development of cancer in experimental studies [33]. In the same way, poor diets characterized as processed and ultra-processed foods rich in refined starches, including products made with white flour such as bread, pasta, and pizza, as well as processed foods high in fat, starches, or sugars which include cakes, candies, and cookies was observed in these studies may be associated to cancer. As a result, these types of diets favor the accumulation of body fat, which can lead to hormonal changes and a chronic inflammatory state. These conditions stimulate cell proliferation, inhibit programmed cell death, and contribute to the formation and progression of several types of cancer, such as stomach adenocarcinoma [7, 9].

This case–control study is subject to limitations. One limitation is associated with the use of the FFQ, which is long and detailed; regarding other questionnaires, interviewees' responses may have been affected by memory bias. Interviewer bias may also affect this type of study, although trained nutritionists interviewed our cases and controls. Despite this potential limitation, the FFQ showed good validity and reproducibility in the estimation of usual food consumption among residents of São Paulo [36]. Moreover, we did not classify the cases as cardia and non-cardia to verify the differences associated with diet, and we opted to not adjust for energy intake according to Smith et al. 2013 [41].

Finally, the type of the food (although processed and ultra-processed) has local and cultural food habits in the Amazon region which are quite different from in São Paulo. However, consumption of processed and ultra-processed foods, especially bread (salted), yellow cheese, fried and roasted meats, fried fish, processed meat, and sweets, were associated independently with the chance of having stomach adenocarcinoma in both cities.

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Data availability Data will be made available on reasonable request.

Code availability Not applicable.

Declarations

Conflict of interest The authors have no conflict of interest to declare. All authors have seen and agree with the contents of the manuscript. We certify that the submission is original work and is not under review by any other publication.

Ethical approval Data described in the manuscript, the codebook, and the analytical codes will be made available upon request and pending approval.

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