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RESEARCH

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# Lack of association between dietary inflammatory index and low impact fractures in the Brazilian population: the Brazilian Osteoporosis Study (BRAZOS)

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## Abstract

**Introduction:** Adequate nutrition, including intake of dietary calcium and vitamin D, is important to maintain bone health. Evidence suggests that a deficiency in micronutrients may contribute to bone loss during aging and exert generalized effects on chronic inflammation. Recently, the *Dietary Inflammatory Index* (DII) was developed to assess the inflammatory potential of individual diets. Our aim was to evaluate the DII in a representative sample and verify its association with low-impact fractures.

**Methods:** Individuals from The Brazilian Osteoporosis Study (BRAZOS) database had their DII calculated. BRAZOS is an important cross-sectional epidemiological study carried out with a representative sample of men and women  $\geq 40$  years old. The research was conducted through in-home interviews administered by a trained team. Nutrition Database System for Research (NDSR) software was used to analyze data on the intake of nutrients, which were employed to calculate the DII using Statistical Analysis Software (SAS®) and Statistical Package for the Social Sciences (SPSS®) to assess its association with low-impact fractures.

**Results:** A total of 2269 subjects had their DII score calculated using information from 24-h recall data. Males had lower DII than females (DII =  $1.12 \pm 1.04$  vs DII =  $1.24 \pm 0.99$ ,  $p = 0.012$ ). Women taking statins had lower DII (DII =  $0.65 \pm 1.14$  vs DII =  $1.26 \pm 0.98$ ,  $p = 0.002$ ), indicating a greater potential for diet-related anti-inflammatory effects.

**Conclusion:** Our findings suggest that women might have a pro-inflammatory diet pattern compared to men. However, we did not find any association between DII scores and low-impact fractures.

**Keywords:** Diet, Inflammation, Low-impact fractures, Osteoporosis, Dietary inflammatory index

## Introduction

Osteoporosis is a systemic skeletal disease characterized by loss of bone mineral density (BMD), impairment of resistance and bone microarchitecture, and higher risk for low-impact fractures [1]. According to the Brazilian Osteoporosis Study (BRAZOS), about 15.1% of women and 12.8% of men reported fragility fractures [2]. More recently, two Brazilian epidemiological studies, SAPOS and SAPORI (Sao Paulo Osteoporosis Study and Sao Paulo

Osteoporosis Risk Index), showed that 33% of postmenopausal women had osteoporosis as diagnosed by Dual-energy X-ray absorptiometry (DXA) measurements, supporting the original findings of BRAZOS [3, 4].

Chronic inflammation is associated with a number of chronic non-communicable diseases (CNCDs), including cancer, cardiovascular diseases, obesity, and diabetes mellitus [5]. It is also related to a higher risk of fractures in women, particularly those with higher CRP [6]. In addition, recent evidence indicates a relationship between oxidative stress and osteoporosis, but its role in fractures is still poorly understood [7, 8]. Therefore, the

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intake of antioxidants could possibly influence BMD in a positive way.

Adequate nutrition, including dietary calcium and vitamin D intake, along with healthy lifestyle changes, are important approaches to minimize bone loss with aging and potential targets for intervention in preventing osteoporosis [9]. Certain micronutrients, including polyphenols, vitamins, polyunsaturated fatty acids (PUFAs), and carotenoids have anti-inflammatory and antioxidant properties [10]. These micronutrients as part of a healthy dietary pattern can help modulate inflammation and oxidative stress and also may be associated with lower CRP levels [11, 12]. Several studies conducted in different populations have shown that the Mediterranean pattern, comprising grains, fruits, vegetables, olive oil, low-fat dairy products, poultry, and nuts, is associated with lower serum levels of CRP and higher plasma levels of adiponectin, suggesting an anti-inflammatory role [13–15]. In contrast, the Western dietary pattern, characterized by a high intake of red meat, high-fat dairy products, and refined grains, is associated with higher CRP serum levels [16].

The Dietary Inflammatory Index (DII®) was developed to provide an overall score of the inflammatory potential of individual diets, based on actual food consumption data, in order to predict levels of inflammatory markers [17]. The DII has been validated with inflammatory markers, including associations with CRP [18, 19], interleukin-6 [20], and homocysteine [21]. It has also been associated with the glucose intolerance and dyslipidemic components of metabolic syndrome [19], asthma [20], and prostate cancer [22].

Recently, three studies have been conducted to examine the relationship between DII scores and fractures [23–25]. The first one was conducted in a large sample of American women, reported finding that high DII scores, indicating a more inflammatory diet, was associated with increased hip fracture risk. However, this finding was limited only to White women [23]. A case-control study in China, confirmed these findings, in both genders, suggesting that pro-inflammatory diet (with lower DII scores) could be positively associated with higher hip fracture risk [24]. More recently, the Osteoarthritis Initiative study, a longitudinal study with a follow-up of 8 years included 3648 participants, showed that higher DII scores were associated with a higher incidence of fractures, but only in women [25].

We hypothesized that DII would be higher, indicating a more pro-inflammatory diet, in individuals with low-impact fractures. This is the first study to evaluate and describe the inflammatory potential of individuals' diets in a representative sample of the Brazilian adult population.

## Material and methods

### Subjects

Data were included from the BRAZOS study. Briefly, BRAZOS is a cross-sectional population-based study

that evaluated age, demographic and anthropometric data, socio-economical aspects, general knowledge about osteoporosis, recurrent falls, medical history, previous fracture, gynecological and reproductive history, familial history of hip fracture after 50 years of age in first-degree relatives, quality of life, current concomitant medication, and comorbidities [2]. Fragility or low-impact fracture was defined as those associated with a fall from standing height or less after age 50 years. Skeletal sites for fragility fractures were axial (ribs, lumbar and thoracic vertebrae) and peripheral bones (forearm, humerus, and femur). Traumatic fractures and those occurring at sites not characteristic of bone fragility (face, skull, tibia, fibula and femoral diaphysis) were excluded from the analysis. Individuals experiencing two or more falls in the previous 12 months were defined as chronic fallers. The presence of cognitive deficiencies (neurological diseases or senile dementia) that could impair the participant's ability to provide informed consent and trustworthy data were excluded from participating in the study. Only one individual >40 years old per domicile was permitted to participate. All participants gave written informed consent prior to participation in the study and the research ethics committee of the Universidade Federal de São Paulo/Escola Paulista de Medicina approved with the protocol number 1738/05.

### Food intake and dietary inflammatory index

To compute the DII, we analyzed data from one 24-h recall interview (24HR). Methods of calculating the DII from the food parameters have been described previously [17]. Briefly, the dietary data were first linked to a world database that provides a robust estimate of mean and standard deviation for each food parameter included in the DII. These parameters then became multipliers to express an individual's exposure relative to the "standard global mean" as a z-score. This was achieved by subtracting the "standard global mean" from the amount reported and dividing this value by the standard deviation. To minimize the effect of right-skewing, this value was then converted to a centered proportion score. The centered proportion score for each food parameter and subject was then multiplied by the respective food parameter effect score in order to obtain a food parameter-specific DII score. All of the food parameter-specific DII scores were then summed to create the overall DII score for each study subject.

DII scores were categorized into sex-specific quartiles. The greater the DII score, the more pro-inflammatory the diet; more negative values represent a more anti-inflammatory pattern. Participants reported food and beverages consumed the day before in detail. The 24HR was administered at home and filled out by an interviewer trained by an experienced nutritionist in this

method. Food data were converted to the respective values of macro and micronutrients using Nutrition Data System for Research version 2005 software (NDSR, University of Minnesota). Energy was adjusted using the residual method described by Willett and Stampfer [26]. Reference values were analyzed considering The Dietary Reference Intakes (DRIs) [27–29] according to age and gender.

In total, 24 of 45 possible food parameters were analyzed to obtain the overall DII score. These included energy intake, carbohydrates, total fat, proteins, cholesterol, saturated fatty acids, monounsaturated fatty acids (MUFAs), PUFAs, fiber, vitamins A, D and E, and minerals such as magnesium, zinc, and selenium.

### Anthropometrics

Body weight (kg) was measured to the nearest 0.1 kg using a balance beam scale after removal of shoes and heavy outer clothing. Height (cm) was measured after removal of shoes using a stadiometer. Height and body weight were used to calculate body mass index (BMI,  $\text{kg}/\text{m}^2$ ). Nutritional status was categorized according to WHO criteria [30].

### Statistical analysis

Data are presented as mean and standard deviation (SD) for continuous variables or as frequency and proportion for categorical variables. Mann-Whitney test was used to compare continuous variables for two groups, and the Kruskal-Wallis test was used for three or more groups, for which multiple comparisons were performed with Mann-Whitney test with Bonferroni corrections. The Chi-square test was conducted to determine the relationship between categorical variables, and Spearman correlation coefficients were computed for continuous variables.

For testing effects on fractures, DII was converted to quartiles based on the frequency distribution in the overall population. Race was dichotomized into 'White' and 'non-White'. BMI was categorized into underweight ( $< 18.5 \text{ kg}/\text{m}^2$ ), normal weight ( $18.5$  to  $< 25.0 \text{ kg}/\text{m}^2$ ), overweight ( $25.0$  to  $< 30.0 \text{ kg}/\text{m}^2$ ), and obese ( $\geq 30.0 \text{ kg}/\text{m}^2$ ) according to WHO classification [30]. Socioeconomic status (SES) was categorized according to the Brazilian Institute of Geography and Statistics (IBGE) [31] as classes A and B (greater or equal to 15 times the minimum wage), C (3 to 5 times the minimum wage), and D and E (1 to 3 times the minimum wage).

Logistic regression analysis models were designed using DII as the independent factor to predict low-impact fractures. All analysis were performed using SPSS® software version 22.0 for Windows (SPSS Inc., Chicago, Illinois). The significance threshold was set at 0.05. The DII scores were calculated using SAS®.

### Results

A total of 2269 individuals had their DII score calculated. We excluded data from 151 participants, mostly women, who had insufficient data or unreliable caloric intake (lower than 500 kcal/day or higher than 5,000 kcal/day). Socioeconomic class, demographics, and lifestyle habits characteristics are shown in Tables 1 and 2. There were no significant differences between genders in terms of race, geographic regions, area, and current smoking status. The mean age of participants was  $59.7 \pm 13.5$  years and was higher among women ( $60.1 \pm 13.7$  years). Most participants were from socio-economic classes D and E (53.8% of total), which correspond to incomes of 1 to 3 times minimum wage (lowest level income).

Current and regular alcohol consumption was significantly higher among males (43.1%) than females (20.6%), with a mean intake of  $4.15 \pm 6.45$  drinks per day (Table 1;  $p < 0.001$ ). Smoking was also significantly higher among men. The prevalence of hypertension, dyslipidemia, osteoporosis, rheumatoid arthritis, and gastritis was higher among women; hence, the use of non-steroidal anti-inflammatory drugs (NSAIDs), statins, and supplements such as calcium and vitamins also were higher in women.

Anthropometric data and food intake are shown in Table 2. According to the WHO classification of BMI (Table 2) 20.9% of females were obese versus 17.9% of males ( $p = 0.01$ ). Energy intake was higher among male subjects compared to females. However, females had a higher intake of carbohydrates ( $p = 0.02$ ) and trans fat ( $p < 0.001$ ). As a result, DII was also higher among females than males ( $p = 0.01$ ) (Table 3).

### Dietary inflammatory index

As shown in Table 3, mean DII score differed significantly between gender, age groups, region, and socioeconomic classes. Males between 50 and 60 years old had lower DII scores than males aged 41 to 50 years and over 71 years ( $p = 0.01$ ). Subjects from South (DII = +1.12) and Central (DII = +1.11) regions had lower scores indicating more anti-inflammatory diets compared to those from the Southeast (DII = +1.19), North (DII = +1.27), and Northeast (DII = +1.36) regions. Males from the Central region had significantly lower scores than those from the South ( $p = 0.03$ ), Northeast ( $p = 0.04$ ) and North ( $p = 0.01$ ). Moreover, females from the South region had lower scores than those from the North ( $p = 0.03$ ) and Northeast ( $p = 0.049$ ). Socioeconomic classes D and E (lowest income) had a higher DII score compared to the other socioeconomic classes (A, B, and C). Males with higher income had lower DII than subjects with lower income.

When DII was converted into quartiles according to gender (Tables 4 and 5), men in quartile 2 were mostly from the Southeast and Central regions ( $p = 0.006$ ).

**Table 1** Demographic and clinical characteristics of the participants – The Brazilian Osteoporosis Study

Characteristic	Total (n = 2269)			Males (n = 684)			Females (n = 1585)			P value
	Mean or n	SD	%	Mean or n	SD	%	Mean or n	SD	%	
Race										0.16
White	1072	–	47.2	308	–	45.0	764	–	48.2	
Non-white	1197	–	52.8	376	–	55.0	821	–	51.8	
Age group										0.03 <sup>a</sup>
40–50 years	785	–	34.6	249	–	36.4	536	–	33.8	
51–60 years	443	–	19.5	152	–	22.2	291	–	18.4	
61–70 years	418	–	18.4	114	–	16.7	304	–	19.2	
≥ 71 years	623	–	27.5	169	–	24.7	454	–	28.6	
Social class <sup>d</sup>										0.03 <sup>b</sup>
AB	314	–	13.8	109	–	15.9	205	–	12.9	
C	735	–	32.4	234	–	34.2	501	–	31.6	
DE	1220	–	53.8	341	–	49.9	879	–	55.5	
Geographic region										0.88
North	297	–	13.1	94	–	13.7	203	–	12.8	
Northeast	475	–	20.9	136	–	19.9	339	–	21.4	
Central-West	330	–	14.5	102	–	14.9	228	–	14.4	
South	372	–	16.4	116	–	17.0	256	–	16.2	
Southeast	705	–	35.0	236	–	34.5	559	–	35.3	
Area										0.68
Metropolitan	1103	–	48.6	328	–	48.0	775	–	48.9	
Interior	1166	–	51.4	356	–	52.0	810	–	51.1	
Marital status										< 0.001 <sup>c</sup>
Single	245	–	10.8	70	–	10.2	175	–	11	
Married	1240	–	54.6	478	–	69.9	762	–	48.1	
Widowed	585	–	25.8	82	–	12.0	503	–	31.7	
Divorced	199	–	8.7	54	–	7.9	145	–	9.2	
Alcohol consumption										< 0.001
Yes	621	–	27.3	295	–	43.1	326	–	20.6	
No	1648	–	72.6	389	–	56.9	1259	–	79.4	
Mean	2.22	4.6		4.15	6.45		1.38	3.17	3.17	< 0.001
Smoking status										< 0.001
Current smoker	438	–	19.3	166	–	24.3	272	–	17.2	
Past	723	–	31.9	269	–	39.4	453	–	28.6	
Never	1108	–	48.8	248	–	36.3	860	–	54.3	
Cigarettes/day	15.12	15.50	–	17.64	14.26	–	13.6	16.07	–	< 0.001
Age started (years)	18.05	11.50	–	15.64	6.87	–	19.5	13.40	–	< 0.001
Age quit (years)	42.75	16.50	–	41.38	14.98	–	43.5730	45	–	0.23
Low impact Fractures										0.006
Yes	205	–	9.0	79	–	11.5	126	–	7.9	
No	2064	–	91.0	605	–	88.5	1459	–	92.1	
Diabetes Mellitus	236	–	7.4	64	–	9.4	172	–	10.9	0.28
Hypertension	790	–	24.6	197	–	28.8	593	–	37.4	< 0.001
Dyslipidemia	175	–	5.5	30	–	4.4	145	–	9.1	< 0.001

**Table 1** Demographic and clinical characteristics of the participants – The Brazilian Osteoporosis Study (*Continued*)

Characteristic	Total (n = 2269)			Males (n = 684)			Females (n = 1585)			P value
	Mean or n	SD	%	Mean or n	SD	%	Mean or n	SD	%	
Osteoporosis	214	–	6.7	21	–	3.1	193	–	12.2	< 0.001
Rheumatoid Arthritis	259	–	8.1	34	–	5.0	225	–	14.2	< 0.001
Cancer	31	–	1.0	10	–	1.5	21	–	1.3	0.8
Gastritis	313	–	13.8	71	–	10.4	242	–	15.3	0.002
Drug therapy										
NSAIDs <sup>e</sup>	85	–	3.7	13	–	1.9	72	–	4.5	0.002
Statins	35	–	1.5	5	–	0.7	30	–	1.9	0.04
Corticoids	94	–	4.1	26	–	3.8	68	–	4.3	0.81
HRT <sup>f</sup>	–	–	–	–	–	–	97	–	6.1	

SD Standard deviation

<sup>a</sup>Difference was observed on 51 – 60 age group ( $p = 0.033$ ), using Bonferroni correction<sup>b</sup>D and E classes had more frequency than the other social classes ( $p=0.014$ )<sup>c</sup>Married and widowed were majority in this study ( $p<0.001$ )<sup>d</sup>Classes A and B (earning 15 times more than minimum wages), C (3 to 5 times minimum wage), and D and E (1 to 3 times minimum wage)<sup>e</sup>NSAIDs: nonsteroidal anti-inflammatory drugs<sup>f</sup>HRT hormone replacement therapy**Table 2** Anthropometric data, food consumption and lifestyle characteristics of the participants

Characteristic	Total (n = 2269)			Males (n = 684)			Females (n = 1585)			P value
	Mean or n	SD	%	Mean or n	SD	%	Mean or n	SD	%	
Weight (kg)	67.30	14.50	–	73.40	14.69	–	64.64	13.67	–	< 0.001
Height (m)	1.59	0.10	–	1.66	0.07	–	1.56	0.09	–	< 0.001
BMI (kg/m <sup>2</sup> )										0.01
Underweight (< 18.5)	69	–	3.0	18	–	2.7	51	–	3.3	
Normal weight (18.5–25)	889	–	39.2	251	–	37.4	638	–	41.1	
Overweight (25–30)	821	–	36.2	282	–	42.0	539	–	34.7	
Obesity (≥30)	444	–	19.5	120	–	17.9	324	–	20.9	
Energy intake (kcal/d)	1335	578	–	1590	698	–	1225	484	–	< 0.001
Carbohydrates (g)	167.9	39.3	–	165.1	47.6	–	169.2	35.0	–	0.02
Proteins (g)	39.3	22.5	–	40.0	26.4	–	39.1	20.7	–	0.9
Lipids (g)	44.2	13.6	–	43.8	15.7	–	44.5	12.6	–	0.28
Trans fat (g)	2.4	2.1	–	2.1	2.1	–	2.6	2.1	–	< 0.001
Saturated fat (g)	13.7	5.9	–	13.5	6.8	–	13.9	5.5	–	0.06
Calcium										< 0.001
Yes	246	–	10.8	47	–	6.9	199	–	12.6	
No	2006	–	88.4	632	–	92.4	1374	–	86.7	
Calcium + Vitamin D	21	–	0.9	3	–	0.4	18	–	1.1	0.11
Vitamins	12	–	0.5	4	–	0.6	8	–	0.5	0.81
Physical activity*										
PEL	1.58	0.76	–	1.68	0.80	–	1.54	0.74	–	< 0.001
AFO	2.38	0.62	–	2.52	0.64	–	2.32	0.61	–	< 0.001
LLA	1.87	0.67	–	2.06	0.75	–	1.79	0.62	–	< 0.001
TS	5.84	1.69	–	6.27	1.77	–	5.65	1.62	–	< 0.001

SD Standard deviation, BMI Body mass index, \*PEL Physical exercises in leisure score, AFO Occupational physical activities, LLA Leisure and locomotion activities, TS Total score overweight was significantly higher in men ( $p < 0.001$ )

**Table 3** Dietary Inflammatory Index according to the characteristics of the participants

Characteristics	DII (n = 2269)								
	Total (n = 2269)			Males (n = 684)			Females (n = 1585)		
	Mean	SD	P value	Mean	SD	P value	Mean	SD	P value
Gender			0.01			–			–
Males	1.12	1.04		–			–		
Females	1.24	0.99		–			–		
Age group			0.006			0.009			0.34
40–50 years	1.25	0.98		1.17	1.00		1.29	0.96	
51–60 years	1.07	1.06		0.93	1.03		1.14	1.07	
61–70 years	1.19	0.98		1.08	1.05		1.23	0.96	
≥ 71 years	1.26	1.01		1.24	1.08		1.28	0.98	
BMI (kg/m <sup>2</sup> )			0.45			0.74			0.4
Underweight (< 18.5)	1.17	1.03		0.87	1.37		1.32	0.81	
Normal weight (18.5–25)	1.17	1.01		1.12	1.05		1.19	1.00	
Overweight (25–30)	1.25	0.99		1.17	1.04		1.30	0.96	
Obesity (≥30)	1.20	1.00		1.12	0.95		1.24	1.01	
Race			0.08			0.52			0.08
White	1.17	0.97		1.10	0.99		1.20	0.96	
Non-white	1.24	1.03		1.13	1.08		1.28	1.01	
Geographic region			0.001			0.006			0.01
South	1.12	1.03		1.16	1.12		1.10	0.99	
Southeast	1.19	0.96		1.11	1.05		1.23	0.92	
Central-West	1.11	0.96		0.84	1.00		1.23	0.92	
North	1.27	1.10		1.29	0.95		1.40	0.97	
Northeast	1.36	0.96		1.19	1.02		1.30	1.12	
Area			0.72			0.23			0.2
Metropolitan	1.17	1.03		1.07	1.03		1.21	1.02	
Interior	1.24	0.98		1.16	1.05		1.28	0.95	
Social class <sup>a</sup>			0.001			0.005			0.02
AB	1.06	1.00		0.81	1.13		1.20	0.89	
C	1.18	1.00		1.17	1.00		1.18	1.00	
DE	1.26	1.00		1.18	1.03		1.29	0.99	
Alcohol consumption			0.81			0.2			0.12
Yes	1.20	1.01		1.08	1.01		1.31	0.99	
No	1.21	1.00		1.15	1.06		1.23	0.98	
Smoking status			0.89			0.86			0.94
Current smoker	1.22	0.96		1.12	1.03		1.28	0.91	
Past	1.19	1.01		1.09	1.05		1.25	0.99	
Never	1.21	1.01		1.15	1.05		1.23	1.00	
Marital status			0.1			0.48			0.25
Single	1.26	1.03		1.12	1.18		1.31	0.96	
Married	1.17	1.02		1.12	1.01		1.21	1.02	
Widowed	1.29	0.95		1.26	1.05		1.29	0.94	
Divorced	1.13	1.15		1.16	1.29		1.11	1.10	

SD Standard deviation, BMI Body mass index

<sup>a</sup>Classes A and B (earning 15 times more than minimum wage), C (3 to 5 times minimum wage), and D and E (1 to 3 times minimum wage)

**Table 4** Characteristics of the participants according to DII quartile for Brazilian men

Characteristics	Quartile 1 ( $\leq +0.49$ )		Quartile 2 ( $+0.49$ a $+1.29$ )		Quartile 3 ( $+1.29$ a $+1.89$ )		Quartile 4 ( $> 1.89$ )		P value
	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	
Age (years)	57.8	12.3	57.5	12.0	58.1	12.9	59.8	14.2	0.6
Weight (kg)	74.2	14.7	74.4	15.3	73.0	13.6	72.0	15.2	0.3
BMI (kg/m <sup>2</sup> )	26.5	4.8	26.4	4.7	26.3	4.3	26.0	4.6	0.86
Alcohol									
Yes	76	45.0	80	46.8	74	43.8	65	37.4	0.31
No	93	55.0	91	53.2	95	56.2	109	62.6	
Mean consumption	7.3	15.5	11.2	22.3	10.3	20.3	6.3	10.8	0.35
Geographic region									0.01
South	27	16.0	24	14.0	25	14.8	39	22.4	
Southeast	54	32.0	67	39.2	62	36.7	53	30.5	
Central-West	31	18.3	37	21.6	18	10.7	16	9.2	
North	22	13.0	16	9.4	27	16.0	29	16.7	
Northeast	35	20.7	27	15.8	37	21.9	37	21.3	
Marital status									0.46
Single	18	10.7	14	8.2	15	8.9	23	13.2	
Married	119	70.4	127	74.3	118	69.8	114	65.5	
Widowed	17	10.1	18	10.5	22	13.0	24	13.8	
Divorced/separated	7	4.1	5	2.9	6	3.6	11	6.3	
Low impact fractures									0.14
Yes	18	10.6	19	11.1	14	8.3	28	16.1	
No	152	89.4	152	88.9	155	91.7	146	83.9	
NSAIDs <sup>a</sup>	2	1.2	5	2.9	4	2.4	13	1.9	0.54
Statins	–	–	3	1.8	–	–	2	1.1	0.15
Hypertension	48	28.4	49	28.7	46	27.2	54	31.0	0.89
Diabetes mellitus	19	11.2	18	10.5	11	6.5	16	9.2	0.46
Osteoporosis	8	4.7	4	2.3	4	2.4	5	2.9	0.54
Dyslipidemia	4	2.4	10	5.8	9	5.3	7	4.0	0.4

SD Standard deviation, BMI Body mass index

<sup>a</sup>NSAIDs Nonsteroidal anti-inflammatory drugs

Nonetheless, for both genders, those with pro-inflammatory potential (quartile 4) were from the South, North, and Northeast ( $p=0.006$ ). Women taking statins had significantly lower DII scores ( $0.65 \pm 1.14$  vs  $1.26 \pm 0.98$ ;  $p = 0.002$ ). Additionally, women on hormone replacement therapy (HRT) tended to have lower DII ( $p = 0.06$ ). However, when analyzed by quartiles, most of the women on HRT were from quartiles 1 and 2 ( $p = 0.03$ ) (Table 5).

### Fractures

Overall, 9% reported low-impact fractures (11.5% of men and 7.9% of women). We did not find any association between low-impact fractures and DII scores. Logistic regression with the DII as an independent variable and fractures as a dependent variable indicated that for every unit increase of the DII score, the chance of having a

low-impact fracture was 1.15 times higher ( $p = 0.08$ ). When adjusted for DM and osteoporosis, we found that for every unit increase of the DII score, the chance of having a low-impact fracture was 1.18 times higher ( $p = 0.08$ ) (data shown only in text). However, these results did not reach statistical significance in either analysis (Table 6).

### Discussion

To the best of our knowledge, this is the first population-based study evaluating the association between DII and fragility fractures in a nationally representative sample. Although females had higher DII scores, indicating pro-inflammatory diets compared to males, we did not find any association with low-impact fractures after multiple adjustments. In Iran, postmenopausal women with

**Table 5** Characteristics of the participants according to DII quartile for Brazilian women

Characteristics	Quartile 1 ( $\leq +0.69$ )		Quartile 2 ( $+0.69$ a $+1.39$ )		Quartile 3 ( $+1.39$ a $+1.93$ )		Quartile 4 ( $> 1.93$ )		P value
	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	
Age (years)	60.7	13.6	59.4	13.8	60.4	14.0	60.4	13.7	0.44
Weight (kg)	64.8	14.3	64.7	13.3	64.0	13.2	65.1	13.9	0.72
BMI (kg/m <sup>2</sup> )	26.2	5.6	26.2	5.2	26.2	4.9	26.6	5.3	0.43
Alcohol									0.35
Yes	76	19.2	73	18.3	88	22.3	89	22.5	
No	320	80.8	325	81.7	307	77.7	307	77.5	
Mean consumption	5.9	17.2	7.5	20.5	5.8	14.8	3.7	7.9	0.16
Geographic region									0.006
South	73	18.4	68	17.1	63	15.9	52	13.1	
Southeast	134	33.8	149	37.4	160	40.5	116	29.3	
Central-West	63	15.9	58	14.6	50	12.7	57	14.4	
North	41	10.4	49	12.3	50	12.7	108	27.3	
Northeast	85	21.5	74	18.6	72	18.2	63	15.9	
Marital status									0.35
Single	41	10.4	39	9.8	45	11.4	50	12.6	
Married	203	51.3	190	47.7	190	48.1	179	45.2	
Widowed	115	29.0	132	33.2	126	31.9	130	32.8	
Divorced/separated	26	6.6	16	4.0	13	3.3	19	4.8	
Low impact fractures									0.15
Yes	37	9.3	35	8.8	21	5.3	33	8.3	
No	359	90.7	363	91.2	374	94.7	363	91.7	
NSAIDs <sup>a</sup>	20	5.1	22	5.5	11	2.8	19	4.8	0.26
Statins	16	4.0	6	1.5	3	0.8	5	1.3	0.003
Hypertension	26	17.2	35	22.6	20	12.7	16	11.3	0.03
Diabetes mellitus	155	39.1	155	38.9	149	37.7	134	33.8	0.38
Osteoporosis	41	10.4	53	13.3	47	11.9	31	7.8	0.08
Dyslipidemia	53	13.4	48	12.1	47	11.9	45	11.4	0.84

SD Standard deviation, BMI Body mass index

<sup>a</sup>NSAIDs Nonsteroidal anti-inflammatory drugs

higher DII scores were more likely to have lower spine BMD measurements [32]. Our findings are similar to the Osteoarthritis Initiative that did not find a statistically significant association between higher DII scores and fractures in men, although it did find higher DII scores in women with fractures [25].

The DII was associated with higher serum levels of CPR in the Seasonal Variation of Blood Cholesterol Study (SEASONS), and CRP of more than 3.0 mg/L was predicted for each one-unit increase in the DII (OR = 1.08; IC = 1.01 to 1.16) based on either 24HR or 7-day recalls [18]. When associated with metabolic syndrome among police officers, DII quartiles 2 to 4 (more pro-inflammatory diets) were more likely to exceed a threshold of 3.0 mg/L for CRP than quartile 1 [19]. In Australia, diet consumed by subjects with asthma was more pro-inflammatory than in healthy controls, and

higher DII was associated with impaired lung function [20]. Higher DII scores, especially in males, also were associated with increased risk of colorectal cancer [23].

Interestingly, the profile of women taking statins in our study was associated with lower DII scores. Although these lower levels can be indicating lower systemic inflammation, the cross-sectional design did not allow us to demonstrate a temporal relationship among these variables [33]. Moreover, low scores may be related to food intake advice given by health professionals and more prospective studies are necessary to establish an effect and causal relationship.

Contrary to our hypothesis, higher BMI was not associated with a more pro-inflammatory diet, emphasizing that some nutrients could have a more positive role in the DII than simply that attributed to total energy consumption and BMI. Considering that nutrients or foods

**Table 6** Dietary Inflammatory Index, according to gender and concomitant diseases

Characteristics	Total (n = 2269)			Males (n = 684)			Females (n = 1585)		
	Mean	SD	P value	Mean	SD	P value	Mean	SD	P value
Low-impact fractures									
Yes	1.22	1.06	0.71	1.28	1.13	0.09	1.18	1.02	0.48
No	1.21	1.00		1.10	1.03		1.25	0.99	
Diseases									
Diabetes Mellitus									
Yes	1.12	0.98	0.07	0.95	1.10	0.14	1.18	0.93	0.19
No	1.22	1.01		1.14	1.04		1.26	1.00	
Hypertension									
Yes	1.18	1.00	0.22	1.12	1.02	0.98	1.19	1.00	0.08
No	1.23	1.01		1.12	1.06		1.28	0.99	
Dyslipidemia									
Yes	1.20	0.97	0.93	1.29	0.89	0.57	1.18	0.99	0.55
No	1.21	1.01		1.12	1.05		1.26	0.99	
Osteoporosis									
Yes	1.18	1.00	0.37	0.96	1.11	0.37	1.20	0.99	0.29
No	1.21	1.01		1.13	1.04		1.26	0.99	
Rheumatoid arthritis									
Yes	1.18	1.01	0.42	1.21	0.75	0.92	1.18	1.05	0.21
No	1.21	1.01		1.12	1.06		1.26	0.98	
Cancer									
Yes	1.21	1.04	0.99	1.17	0.89	0.99	1.23	1.12	0.99
No	1.21	1.01		1.12	1.05		1.25	0.99	
Gastritis									
Yes	1.21	1.01	0.83	1.17	1.03	0.67	1.22	1.00	0.5
No	1.21	1.01		1.12	1.05		1.25	0.99	
Asthma									
Yes	1.16	1.02	0.78	1.32	0.92	0.17	1.08	1.06	0.2
No	1.21	1.01		1.11	1.05		1.26	0.99	
Drug therapy									
NSAIDs <sup>a</sup>									
Yes	1.23	1.04	0.66	1.20	0.67	0.91	1.24	1.09	0.54
No	1.21	1.01		1.12	1.05		1.25	0.99	
Statins									
Yes	0.75	1.11	0.009	1.32	0.74	0.76	0.65	1.14	0.002
No	1.22	1.01		1.12	1.05		1.26	0.98	
Corticoids			0.5			0.06			0.95
Yes	1.10	1.04		0.70	1.05		1.26	1.00	
No	1.22	1.01		1.14	1.03		1.25	0.99	
Premenopausal	–			–			1.26	0.98	0.49
Menopausal	–			–			1.21	0.98	0.25
HRT <sup>b</sup>	–			–					0.06

**Table 6** Dietary Inflammatory Index, according to gender and concomitant diseases (Continued)

Characteristics	Total (n = 2269)			Males (n = 684)			Females (n = 1585)		
	Mean	SD	P value	Mean	SD	P value	Mean	SD	P value
Yes	–			–			1.02	1.09	
No	–			–			1.25	0.95	
Calcium			0.64			0.87			0.66
Yes	1.39	0.98		1.17	0.90		1.32	1.00	
No	1.21	0.98		1.12	1.05		1.25	0.99	

SD Standard deviation

<sup>a</sup>NSAIDs Nonsteroidal anti-inflammatory drugs<sup>b</sup>HRT Hormone replacement therapy

are rarely eaten in isolation, dietary patterns may have synergistic or antagonistic biochemical interactions among nutrients as well as different food sources of the same nutrient. Instead of looking at individual nutrients or foods, pattern analysis examines the effects of the overall diet. Conceptually, dietary patterns represent a broader picture of food and nutrient consumption and may be more predictive of higher risk of diseases than the individual intake of foods or nutrients [34, 35].

Our previously published studies have shown some relationships between nutrient intake and osteoporotic fractures such as consumption of antioxidants [36], and caffeine [37], as well as clinical risks factors for fractures [2], recurrent falls [38], and quality of life [39]. Consumption of solid fats and added sugars (SoFAS) in Brazil corresponds to 52% of daily intake, and they are provided from food with empty calories, especially in women and teenagers [40]. This outcome also was observed in our study. Women from BRAZOS had a higher consumption of carbohydrates and trans fat compared to men, resulting in higher DII scores.

A possible explanation for the association between DII scores and lower income could be explained by the inadequate consumption of fruits and vegetables, which tend to be expensive. According to Sichieri and colleagues [41], the traditional pattern is mostly determined by socioeconomic conditions, and apart from that, is a protection for overweight and obesity. However, the antioxidant intake was low in the adult Brazilian population [36], regardless of social class, economic status, race, or region of the country.

The latest Household Budget Survey report describing food intake of the Brazilian population also showed a positive association between consumption of vegetables and fruits and socio-economic classes and a negative association with manioc flour [42]. Fruits, vegetables, skim milk, and dairy intake increased proportionately to higher income. When categorized by the 5 regions of Brazil, the Central region, which had the lowest DII scores (most anti-inflammatory) in our study, had a higher consumption of rice, beans, red meat, and grains.

The South region, with the second lowest DII scores in our study, had a higher consumption of tea, dairy products, vegetables, salad, fruits, and meat. The North and Northeast, with higher DII values, had a significantly higher intake of flour, pasta, and starch. All of these findings related to regional differences may be explained by the history of colonization (Italy and German in the South and Southeast and Portugal in the Northeast, for instance) and lifestyle in this huge continental country [43].

### Limitations and perspectives

Our study has some limitations, such as a lack of measurements of CRP serum levels or other inflammatory biomarkers for comparison with the DII. However, previous studies regarding the DII have shown its ability to estimate CRP levels in other populations. Furthermore, we did not perform any spine radiograph to evaluate morphometric vertebral fractures or DXA measurements for diagnosis of osteoporosis. Also, its cross-sectional design and use of one 24-h recall interview pose another limitation. Another limitation of the 24-h recall is that only 24 out of the 45 food parameters were available for calculating DII scores. It is likely that the results would have been better with more food parameters, such as flavonoids, ginger, onions, and garlic. Further studies with larger sampling size and longitudinal design, particularly intervention clinical trials, are needed to establish the association between the DII and low-impact fractures.

### Conclusions

In Brazil, food consumption is basically represented by energy-dense, nutrient-sparse foods, contributing to a higher pro-inflammatory potential. In the present study, women had a higher DII compared to men. We did not find any associations with higher DII and low impact fractures. The profile of women taking statins in this study was associated with diet pattern that were potentially anti-inflammatory. Additionally, because of the cross-sectional design of this study, we are not able to establish a causal relationship.

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## Availability of data and materials

Database is available upon request.

## Authors' contributions

MMP and LAM: were responsible for the study design, statistical analysis and the elaboration of the paper; NJS: performed all the nutrient calculation and participated in paper elaboration; PSG: participated in the nutrient calculation and conducted training about 24 h-R for interviewers. NS: performed the Dietary Inflammatory Index calculation; MM: database review and nutrients reassessment for Dietary Inflammatory Index calculation, statistical analysis, results from analysis and elaboration of the paper. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

All participants gave written informed consent prior to participation in the study and the research ethics committee of the Universidade Federal de São Paulo/Escola Paulista de Medicina approved with the protocol number 1738/05.

## Consent for publication

Not applicable.

## Competing interests

Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina in order to develop computer and smartphone applications for patient counseling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI. The subject matter of this paper will not have any direct bearing on that work, nor has that activity exerted any influence on this project. The authors have no other potential competing interest to disclose.

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