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OBSERVATIONAL STUDY ON METABOLIC PATTERNS AND DIET IN FEMALE PATIENTS UNDERGOING FOLLOW-UP PROGRAM FOR BREAST CANCER

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Summary

Abstract

Introduction: The prevalence of the metabolic syndrome (MS) is increasing worldwide at any age, exposing the populations at risk of major health problems: diabetes mellitus, obesity, hypertension, cardiovascular diseases, and cancer. Several trials have shown that obesity is a risk factor for several malignancy, including breast cancer. Breast cancer is one of the most frequently diagnosed malignancy, counting over a million cases each year, and the leading cause of cancer death in women worldwide.

Physical activity and mediterranean diet represent protective factors that may reduce breast cancer recurrence. We aimed to assess lifestyle habits in two groups of subjects (i.e., BCS, breast cancer survivors in follow-up (<6 mo.); CG, females without breast cancer).

Materials and Methods: between September 2015-June 2016, 100 BCS subjects and 100 CG subjects were enrolled (age 55±3.3 vs. 53±1.2 yrs, P=NS).

The protocol included a brief physical examination (history, waist circumference with cut-off values for visceral adiposity by IDF and ATPIII, Body Mass Index - BMI), administration of a specific custom-designed questionnaire (MEDSTYLE) and use of Winfood® software (Medimatica, Teramo, Italy) for assessing basal metabolic rate, physical activity, daily average diet, "junk food" consumption, smoking and drinking habits.

Results: Waist circumference was greater in BCS than CG (IDF 89.7±4.7 cm vs. 80.1± 2.2, P<0.0001; ATPIII 104.6±3.5 vs. 90.3±4.1 cm, respectively, P<0.0001). Body mass index (BMI) was greater in BCS than CG (25.8±1.8 vs. 21.3±0.8 cm, respectively, P<0.0001).

Overall, daily caloric intake was 1412±25 Kcal in CG vs 1833±40 Kcal in BCS (P<0.000001) gained across 4.3±0.1 meals. Prevalence of cigarette smoking (14.4% vs. 19.1%) and alcohol consumption (76.5% vs. 62.2%, P=0.056) tended to be lower in CG than in BCS. Number of weekly alcoholic drinks were 2.0±0.3 in CG and 2.2±0.3 in BCS. Sedentary life was similar between CG and BCS

(60.0% vs 51.5%). In those performing physical activity, the number of weekly activities were 2.7±0.2 for 88±8 Kcal/d in CG and 2.5±0.2 for 113±14 Kcal/d in BCS (P=NS). Daily consumption of extravirgin olive oil was greater in BCS than in CG (38.7 ±3.4 vs. 23.3±1.0 g/day, P<0.0001). Intake of solid-liquid junk (fast) food based on a frequency-size 7-items composite score, was greater in BCS than CG (19.3±0.8 vs. 16.8±0.6, P=0.015) and tended to correlate positively with abdominal girth in the whole group (r=+0.28; P=0.052). Although the frequency of legumes consumption was comparable, the score for size of legume intake was significantly smaller in CG than BCS (1.6±0.07 vs 1.9±0.09, P=0.0028).

Protein intake (red meat >poultry>fish) did not respect the international recommended guidelines (50 g/d) and was higher in BCS than in CG (67.3±10.9 vs. 88.8±14.6, P<0.001). Fiber consumption was low, lower in CG than BCS (14.4±0.25 vs.15.8±0.4 g/day, P=0.0038)

Conclusions: this survey provides a consistent anthropometric and lifestyles database in two groups of middle-aged women living in Apulia, Italy, a typical Mediterranean region. Breast cancer survivors display a “dysmetabolic” profile, with increased visceral fat-overweight-obesity, high intake of proteins, junk food, and sedentary life.

Although the area of enrollment was a mediterranean region, both groups showed low adherence to mediterranean diet with low intake of fiber and high intake of red meat.

Hazardous habits and metabolic profile can be dangerous in subjects at “high” risk (previous history of cancer). Educational healthy programs are mandatory in the general and in “selected” populations.

INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy worldwide in women, showing the highest incidence rates in North America, Australia/New Zealand, and in western and northern Europe, and lowest in Asia and sub-Saharan Africa [1-4]. The different incidence between countries is likely related to societal changes (i.e., changes in fat intake, body weight, age at menarche, and/or lactation, and reproductive patterns such as fewer pregnancies and later age at first birth). Studies of migration patterns in the USA point on the importance of cultural and/or environmental changes [1].
About one-half of newly diagnosed breast cancers can be explained by known risk factors (i.e., age at menarche, first live birth, menopause, and proliferative breast disease). An additional 10 percent are associated with a positive family history. In addition, risk may be modified by demographic, lifestyle, and environmental factors, although their association with breast cancer risk has not been clearly demonstrated.

Many early breast carcinomas are asymptomatic; pain or discomfort is not usually a symptom of breast cancer. Breast cancer is often first detected as an abnormality on ETG (EcoTomoGraphy) or a mammogram before it is felt by the patient or healthcare provider.

The general approach for evaluating breast cancer includes a triple assessment: clinical examination, imaging (usually mammography, ultrasonography, or both), and needle biopsy. Early diagnosis is available thanks to an increased public awareness and improved screening. Moreover, amelioration in therapy and screening has produced an improvement in survival rates for women with breast cancer.

Over the past 3 decades, extensive and advocate-driven breast cancer research has led to extraordinary progress in the understanding of the disease.

Several modifiable risk factors in the development of newly breast cancer and its recurrence have been identified.

Obesity is associated with an overall increase in morbidity and mortality. The "Body mass index (BMI)" is a simple index which classifies individuals according to weight-for-height (kg/m2) and splits in different metabolic categories (**Table 1**). A BMI greater than 30 kg/mt2. The prevalence of overweight and rising is increasing worldwide, and is generally greater among women than among men in all age brackets (**Figure 1**).

Impressive numbers appear from the recent WHO global. In fact more than 1.9 billion adults are overweight, and of these over 650 million adults are obese (http://www.who.int/mediacentre/factsheets/fs311/en/).

The problem is that the worldwide prevalence of obesity dramatically tripled between 1975 and 2016, and this trend is more pronounced in civilizated population.

Overweight and obesity are strongly linked to death and disability in industrialized states, and represent an important public health problem worldwide.

The cause of obesity and overweight is more than the imbalance between calories intake and calories expended, but depends on a complex interaction between genetic, epigenetic and environmental factors. Environmental changes include an increased sedentary lifestyle and a great availability and consumption of energy dense foods.

The consequence of obesity is a major risk factor for several diseases, including heart disease and stroke, diabetes, musculoskeletal disorders (especially osteoarthritis), several cancers (breast, ovarian, prostate, liver, gallbladder, kidney, and colon).

A study by Calle showed that obesity is associated with an increased risk of breast cancer in women, especially in postmenopausal population [(5)]. However, the molecular mechanisms linking obesity to breast cancer are not totally understood. One important factor contributing to obesity–breast carcinogenesis might be represented by an excessive exposure of mammary epithelium to various molecules produced by the adipose tissue (adipokines). Indeed, adipose tissue contributes to the production of estrogens, insulin and insulin-like growth factors, all of which are likely involved in mammary tumorigenesis [(6)].

The presence of obesity at the time of breast cancer diagnosis represents a poor prognostic factor (**Table 2**) and is indipendent by racial/ethnic component. Obesity may impact the outcomes in women with HER2 positive cancer and likely plays a role in outcomes in women with hormone-receptor positive breast cancer [(7)]. This finding might be explained by the higher estrogen levels in obese women with hormone-receptor positive tumors (risk estimate, 1.82; 95% CI, 1.55 to 2.14 for overweight and obese combined) [(8)] (**Figure 2**). Most concerning is evidence that obese women do not display the same protection from aromatase inhibitors when compared with normal weight women. Other contributing factors in the relationship between obesity and poor breast cancer outcomes are represented by an altered glucose metabolism and the presence of metabolic syndrome and type 2 diabetes[(7)].

Obese patients display larger tumors, increased lymph node metastases and higher-grade tumors [(9, 10)].

The higher T and N stages in obese women may also represent a more aggressive biological behaviour which lead to higher risk of recurrence. In fact, when adjusting for these tumor factors, overweight and obesity remain independent risk factors for decreased breast cancer–specific survival and overall survival.

Sedentary lifestyle is strongly linked to obesity, and has been associated with higher risk of breast cancer regardless of menopausal status [(11)].

Alcohol consumption is associated with an increased risk of breast cancer with a dose-response relationship. By contrast, a mediterranean diet, characterized by an abundance of plant foods, fish, and olive oil, may decrease the risk of developing breast cancer.

This was showed by a secondary analysis of a clinical trial of over 4000 women (age range 60-80 years) who were randomly assigned to a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat) with a primary outcome of cardiovascular disease [(12)]. Compared with the control group, at a median follow-up of 4.8 years, women consuming a Mediterranean diet supplemented with extra-virgin olive oil experienced a lower breast cancer rate (hazard ratio [HR] 0.32, 95% CI 0.13-0.79).

Women consuming a Mediterranean diet supplemented with nuts experienced a trend towards decreased breast cancer rates (HR 0.59, 95% CI 0.26-1.35).

The analysis of alimentary risk factors may result hard, because data regarding the contribution of micronutrients on breast cancer risk are inconclusive or modest.

According to the ACS/ASCO Obesity Breast Cancer Care Guidelines (**Table 3**), reccomendations in breast cancer survivors include the achievement of healthy weight, the promotion of physical activity, and the achievement of dietary pattern based on vegetables, fruits, whole grains, and legumes [(13, 14)].

AIMS OF THE STUDY

Based on these observations, we aimed to study lifestyle and alimentary patterns in a cohort of female patients in follow-up for breast cancer compared with control group. Moreover, we aimed to identify the presence of metabolic syndrome and/or other metabolic disturbances.

The identification of “bad” dietary habits may guide the follow-up program in order to include healthy eating in the prevention of breast cancer recurrence.

MATERIALS AND METHODS

Between September 2015-June 2016, 100 females breast cancer survivors (BCS) in follow-up (<6 mo.) undergoing bone scintigraphy and 100 females without breast cancer (CG) were enrolled (age 55±3.3 vs. 53±1.2yrs, P=NS).

Inclusion criteria: a previous diagnosis of breast cancer. Patients were screened and enrolled from those who underwent bone scintigraphy for followup for suspicion of bone metastasis at the "OO.RR." Nuclear Medicine Unit in Foggia.

Exclusion criteria

Patients with evidence of bone metastasis at the bone scintigraphy

Bone scintigraphy: operative procedure

The first step was the patient evaluation including the assessment of blood tests and previous bone scans. Subsequently, the patient was provided with an informative note and informed consent.

In the SPECT room, after disinfection of the volar face of the forearm, the patient will be injected ^{99m}Tc-HDP with a 2.5 ml syringe. The radiopharmaceutical activity is 740 MBq.

Finally, a compressive dressing is applied. Basically, the procedure is followed by a waiting period in a screened room, according to the provisions of Legislative Decree 187/2000 concerning radiation protection.

The patient is then invited to drink more than a liter of water to eliminate the proportion of radiopharmaceutical not bound to the bone tissue and empty the bladder with a pre-scintigraphy urination.

After 150 minutes from the injection, the patient undergoes a total body scintigraphy with the gamma camera Model 630 General Elettric. At the end of the exam, it will be sent out through an obligatory path established according to the operative procedures in force.

Study design

As shown in **Figure3**, subjects were evaluated at baseline (week 0, T0).

After initial evaluation, including history and a general physical examination, subjects signed the informed consent form and were enrolled in one of the two study groups.

At baseline (T0), all subjects underwent the measurement of anthropometric data, including BMI and visceral adiposity.

Anthropometric data

The body mass index (BMI) was calculated as body weight (in kg) ÷ height (in meters) squared. Overweight was defined as a BMI ≥25.0 to 29.9 kg/m2; obesity was defined as a BMI ≥30 kg/m2. Waist circumference, a marker of abdominal (visceral) obesity, was calculated according to ATPIII and IDF criteria (≥102 cm for men and ≥88 cm for women and ≥94 cm for men and ≥80 cm for women according to ATPII and IDF, respectively).

Assessment of alimentary habits

A specific custom-designed questionnaire (MEDSTYLE) was used to evaluate lifestyles and daily intake of foods. Medstyle is a custom-designed questionnaire adapted from previous validated alimentary questionnaires [(15, 16)] was tested across different age, and anthropometric groups in health and disease [(17,18, 19)] and consists of 35 food items (156 foods). Questions focused on frequency (day, week or month) and portion sizes (small, medium and large, represented by colour pictures) of food consumption.

To assess the consumption of junk food it has been attributed a so called "junk score" derived from the sum of the portions and frequency of different junk foods. This score is a measure of the consumption of fast food (sweet snacks, salty snacks, pastry, chips, soft drinks and fruit juices) (**Table 4**).

The software WinFood® (Medimatica, Teramo, Italy)was used to assess nutrient composition of the foods, basal metabolic rate, physical activity, daily average diet, "junk food" consumption, smoking and drinking habits.

Sedentary lifestyles

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure. Physical activity can be measured by direct observation, assessment of energy expenditure (e.g., doubly labeled water technique), diaries, questionnaires and performance-based motion sensors (e.g., pedometers and accelerometers) [20,21]. The recommended minimum amount of physical activity for adults to promote and maintain physical health is 30 min of moderately intense aerobic physical activity at least 5 days a week or 20 min of vigorously intense aerobic physical activity at least 3 days a week, or an equivalent combination[22].

Patients were defined as sedentary if present any weaking behavior characterized by an energy expenditure ≤1.5 metabolic equivalents (METs) or aerobic physical activity < 30 min at least 5 days a week or 20 min of vigorously intense aerobic physical activity at least 3 days a week.

Statistical analysis

Results are given as means±SEM. Variables were checked for normal distribution (Kolmogorov-Smirnov goodness of fit test). Contingency tables were evaluated by chi-squared or Fisher's exact tests. Comparison of continuous variables among groups was performed with unpaired student's t-tests or Mann-Whitney rank sum tests. The relationship between variables was analysed by Spearman's correlation coefficient. Statistical analyses were carried out using the *NCSS* software package (NCSS 9 Statistical Software 2013. NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/ncss) [23]. A P-value of less than 0.05 was considered statistically significant.

RESULTS

As shown in **Table 5**, the final cohort included 100 females breast cancer survivors (BCS) in follow-up (<6 mo.) undergoing bone scintigraphy and 100 females without breast cancer (CG) (age 55±3.3 vs. 53±1.2yrs, P=NS). In 20% of BCS, a family history of breast cancer was recorded.

Body mass index (BMI) was greater in BCS than CG (25.8±1.8 vs. 21.3±0.8 cm, respectively, P<0.0001). Waist circumference was greater in BCS than CG (IDF 89.7±4.7 cm vs. 80.1± 2.2, P<0.0001; ATPIII 104.6±3.5 vs. 90.3±4.1 cm, respectively, P<0.0001).

Waist circumference correlated positively and significantly with BMI (r=0.8, P<0.0001).

Overall, daily caloric intake was 1833±40 Kcal in BCS vs 1412±25 Kcal in CG (P<0.000001) gained across 4.3±0.1 meals (**Figure 4**).

Prevalence of cigarette smoking (14.4% vs. 19.1%) and alcohol consumption (76.5% vs. 62.2%, P=0.056) tended to be lower in CG than in BCS (**Figure 5**).

Number of weekly alcoholic drinks were 2.2±0.3 in BCS and 2.0±0.3 in CG.

Sedentary life (i.e. no consistent weekly physical activity) was similar between BCS and CG (51.5% vs 60.0%). In those performing physical activity, n. of weekly activities were 2.5±0.2 for 113±14 Kcal/d in BCS and 2.7±0.2 for 88±8 Kcal/d in CG (P=NS).

Daily consumption of extravirgin olive oil was greater in BCS than in CG (38.7 ±3.4 vs. 23.3±1.0 g/day, P<0.0001) (**Figure 6**).

Intake of solid-liquid junk (fast) food based on a frequency-size 7-items composite score, was greater in BCS than CG (19.3±0.8 vs. 16.8±0.6, P=0.015) (**Figure 7**) and tended to correlate positively with abdominal girth in the whole group (r=+0.28; P=0.052).

Although the frequency of legumes consumption was comparable, the score for size of legume intake was significantly greater in BCS than CG (1.9±0.09 vs 1.6±0.07, P=0.0028) (**Figure 8**).

Fiber consumption was low, greater in BCS than CG (15.8±0.4 vs 14.4±0.25 g/day, P=0.0038) (**Figure 9**).

Protein intake (red meat >poultry>fish) did not respect the international recommended guidelines (50 g/d) and was higher in BCS than in CG (88.8±14.6 vs 67.3±10.9, P<0.001) (**Figure 10**).

DISCUSSION

In this observational study we show that the group including breast cancer survivors (BCS) displayed a dysmetabolic profile when compared with control subjects.

The presence of obesity and increased waist circumference in BCS is expression of visceral adipose tissue. It is note that visceral obesity increases the cardiovascular risk and the susceptibility to malignancies [24, 25]. Visceral adipose tissue is a hormonally active tissue, since it produces bioactive molecules and hormones, including leptin, tumour necrosis factor (TNF), adiponectin, resistin and interleutin 6 (IL-6). Adiponectin displays a protective antiangiogenic activity. When the aumount of visceral adipose tissue increases, the circulating adiponectin decreases leading to a promotion of Type 2 diabetes, hypertension, elevated glucose levels, cardiovascular disease and malignancies [26].

Overweight and obese BCS have lower survival when compared with normal weight women. One explanation is that the increased degrees of visceral adiposity leads to higher concentrations of tumor-promoting hormones [27].

Moreover, the risk of recurrence of breast cancer is strongly linked to the hormonal and biological factors which are produced by visceral adipose tissue (i.e., estrogens, sex hormone binding globulin (SHBG), insulin, and leptin) [28].

Based on these observation, it is clear that the identification of obesogenic profile of our BCS group is necessary. The reduction of body weight and visceral adiposity is mandatory in BCS and may represent a strategy for the prevention of breast cancer recurrence.

We wanted to profile a group of breast cancer survivors living in a typical mediterranean regione, namely Apulia. Although our patients had a great availability of fresh typical mediterranean products, they showed alterations in caloric intake and in quality of diet.

The main findings are represented by the increased daily amount of calories. In BCS the daily consumption of extravirgin olive oil was double respect to that recommended by the US FDA's statement(2 tablespoons (23 grams) of olive oil daily).

When looking to the “good” alimentary pattern of the mediterranean diet, our patients showed an excessive intake of “good” calories which became “bad” and inappropriate for their metabolism and energy demand.

On the other hand, we looked at the “bad” lifestyle, including the consumption of junk foods, the higher intake of protein, and the physical inactivity. Junk foods consumption are “unhealthy” foods, because are typically high in kilojoules, fat, saturated fat, sugar, and salt. Furthermore junk foods are associated with increased BMI, visceral adiposity, and insulin resistance [(29)]. Previous studies have shown that junk food consumption is linked to other unhealthy eating behaviors[(30)].

Junk foods represent a hazardous alimentary pattern and its consumption represents a risk factor for metabolic disturbances and breast cancer recurrence.

Although breast cancer survivors consumed more fiber than control subjects, the amount was not appropriate according to international guidelines. In fact, fiber intake was lower than the American Heart Association Eating Plan suggestions (25-30 grams/day).

The analysis of habits in our breast cancer survivors show a dangerous picture. The geographical area offers the best alimentary products, but survivors do not know how to manage food resources and have not been educated on the pros and cons of qualitative and quantitative choices.

It is necessary a health policy to give information on healthy life style during followup and to correct bad alimentary pattern which may decrease the survival.

CONCLUSION

Obesity and excess adipose tissue are risk factors for breast cancer recurrence in postmenopausal women, and are linked to poor prognosis following the diagnosis and treatment of breast cancer.
Breast cancer survivors show a metabolic profile and dangerous lifestyle (i.e., sedentary habits and diet patterns, such as a hypercaloric and/or low-quality diet) that can decrease the survival.
The findings of this study show that reduction of weight loss and adipose tissue is mandatory and can be achieved through healthy programs of alimentary education. A healthy lifestyle is an easy, sustainable and exportable strategy to improve outcomes in obese women with breast cancer.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to Sergio Modoni, MD,Head of the Nuclear Medicine Unit of “OO.RR.” of Foggia and Leonilde Bonfrate, MD, PhD, Internist Doctor, for the continuous support of my Ph.D study.

TABLES

Table 1: The International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI(kg/m^2)	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004.

Table 2: BMI and Breast Cancer Prognosis: Meta-Analyses (Adapted by Jiralerspong S et al., J Clin Oncol. 2016)

Table 1. BMI and Breast Cancer Prognosis: Meta-Analyses

Study	Year Published	Setting	Study Design	Country	Patient Types	No. of Patients	Time Period	Follow-Up	Chemotherapy	Endocrine Therapy	Results
Protani[10]	2010	NA	Meta-analysis of 43 studies	International	All subtypes; node positive or negative	NA	1963-2005	4-14 years	NA	NA	Worse OS (HR, 1.33; 95% CI, 1.21 to 1.47) and BCSS (HR, 1.33; 95% CI, 1.19 to 1.50) in obese *v* nonobese patients No significant differences by menopausal status, year of diagnosis, or treatment *v* observational cohort
Niraula[11]	2012	NA	Meta-analysis of 21 studies	International	All subtypes; node positive or negative	80,326	NA	5-20 years	NA	NA	Worse OS in overweight or obese patients in ER-positive (HR, 1.31; 95% CI, 1.17 to 1.46) and ER-negative subsets (HR, 1.18; 95% CI, 1.06 to 1.31) Worse OS in overweight or obese patients in premenopausal (HR, 1.23; 95% CI, 1.07 to 1.42) and postmenopausal subsets (HR, 1.15; 95% CI, 1.06 to 1.26) Worse BCSS in overweight or obese patients in ER-positive (HR, 1.36; 95% CI, 1.20 to 1.54) and ER-negative subsets (HR, 1.46; 95% CI, 0.98 to 2.19) Worse BCSS in overweight or obese patients in premenopausal (HR, 1.18; 95% CI, 0.82 to 1.70) and postmenopausal subsets (HR, 1.38; 95% CI, 1.11 to 1.71) No significant differences between ER-positive and ER-negative disease or between pre- and postmenopausal patients for any of the above
Chan[12]	2014	NA	Meta-analysis of 82 studies	International	All subtypes; node positive or negative	213,075	1957-2009	≥ 5 years for all but eight studies	NA	NA	Poorer total mortality (HR, 1.41; 95% CI, 1.29 to 1.53) and breast cancer–specific mortality (HR, 1.35; 95% CI, 1.24 to 1.47) for obese *v* normal-weight patients Poorer total mortality (HR, 1.07; 95% CI, 1.02 to 1.12) and breast cancer–specific mortality (HR, 1.11; 95% CI, 1.06 to 1.17) for overweight *v* normal-weight patients

Abbreviations: BCSS, breast cancer–specific survival; BMI, body mass index; ER, estrogen receptor; HR, hazard ratio; NA, not applicable; OS, overall survival.

Table 3: ACS/ASCO Obesity Breast Cancer Care Guidelines

Table 6. ACS/ASCO Obesity Breast Cancer Care Guidelines[96,97]

Guideline
Obesity
It is recommended that clinicians counsel survivors to achieve and maintain healthy weight and if overweight or obese to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss
Physical activity
It is recommended that clinicians counsel survivors to engage in regular physical activity consistent with the ACS guideline[96] and specifically avoid inactivity and return to normal daily activities as soon as possible after diagnosis, aim for ≥ 150 minutes of moderate or 75 minutes of vigorous aerobic exercise per week, and include strength training exercises ≥ 2 days per week and emphasize strength training for women treated with adjuvant chemotherapy or hormone therapy
Nutrition
It is recommended that clinicians counsel survivors to achieve a dietary pattern that is high in vegetables, fruits, whole grains, and legumes; low in saturated fats; and limited in alcohol consumption

Abbreviations: ACS, American Cancer Society.

Table 4: Junk food score according to type, frequency and portion of foods

7 ITEMS
Chips
Fried Potatoes
Sweet Snacks
Bakery Products
Salt Snacks
Soft Drinks
Fruit Juice

FREQUENCY	SCORE
NEVER	0
RARELY	1
ONCE A WEEK	2
2-3 TIMES A WEEK	3
4-5 TIMES A WEEK	4
DAILY	5

PORTION	SCORE
SMALL	1
MEDIUM	2
LARGE	3

Table 5: Characteristics of enrolled subjects

	BCS (N=100)	CG (N=100)	P
Age (yrs)	55±3.3	53±1.2	NS
BMI (mt2/kg)	25.8±1.8	21.3±0.8	0.0001
IDF (cm)	89.7±4.7	80.1±2.2	0.0001
ATP (cm)	104.6±3.5	90.3±4.1	0.0001
N. Crit. SMET	1.6±0.4	-	-
Type of surgery	60% quadrantectomy; 40% radical mastectomy	-	-
Familial history of breast cancer	20%	-	-

FIGURES

Figure 1: Prevalence of Obesity at the Global Level, According to Sociodemographic Index (SDI) (Adapted by N Engl J Med 2017;377:13-27).

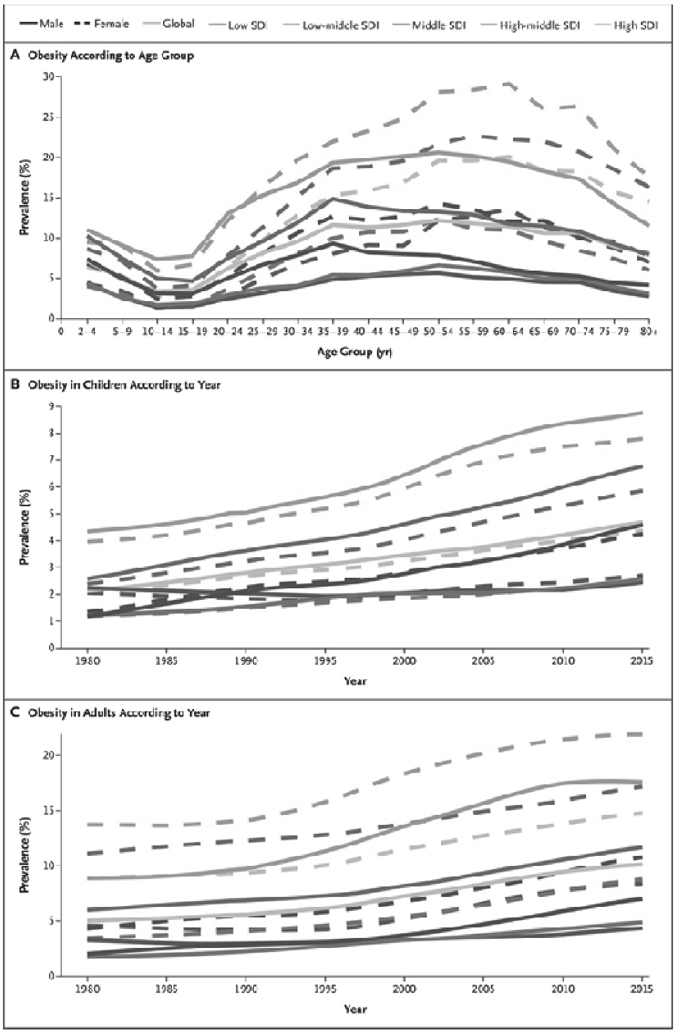


Figure 2: Different mechanisms of estrogen dependence for hormone related breast cancer in premenopausal and in postmenopausal women (Adpted by Maccio' A et al., J Mol Med 2010)

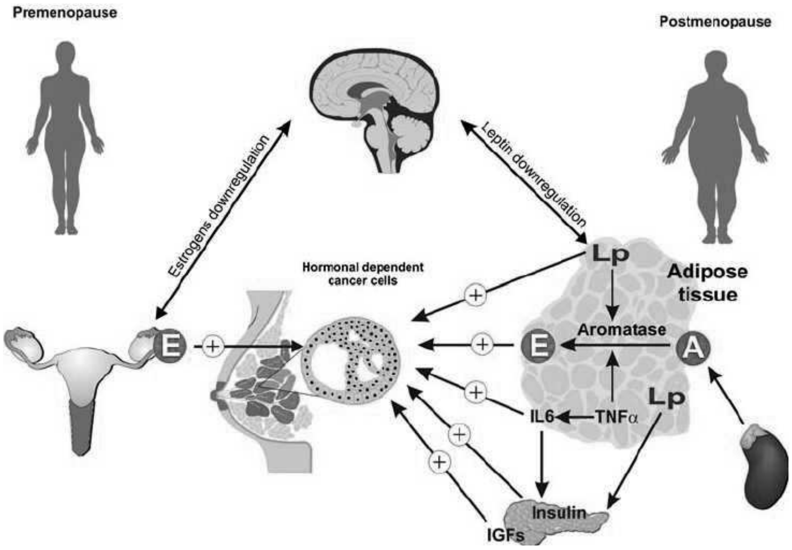


Figure 3: Study design

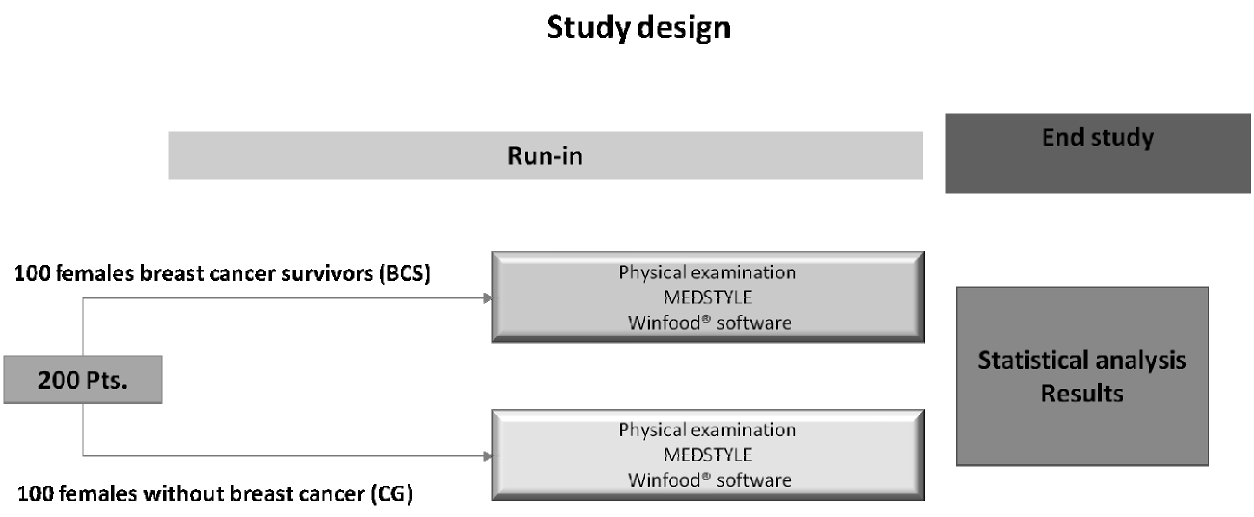


Figure 4: Daily caloric intake in two groups

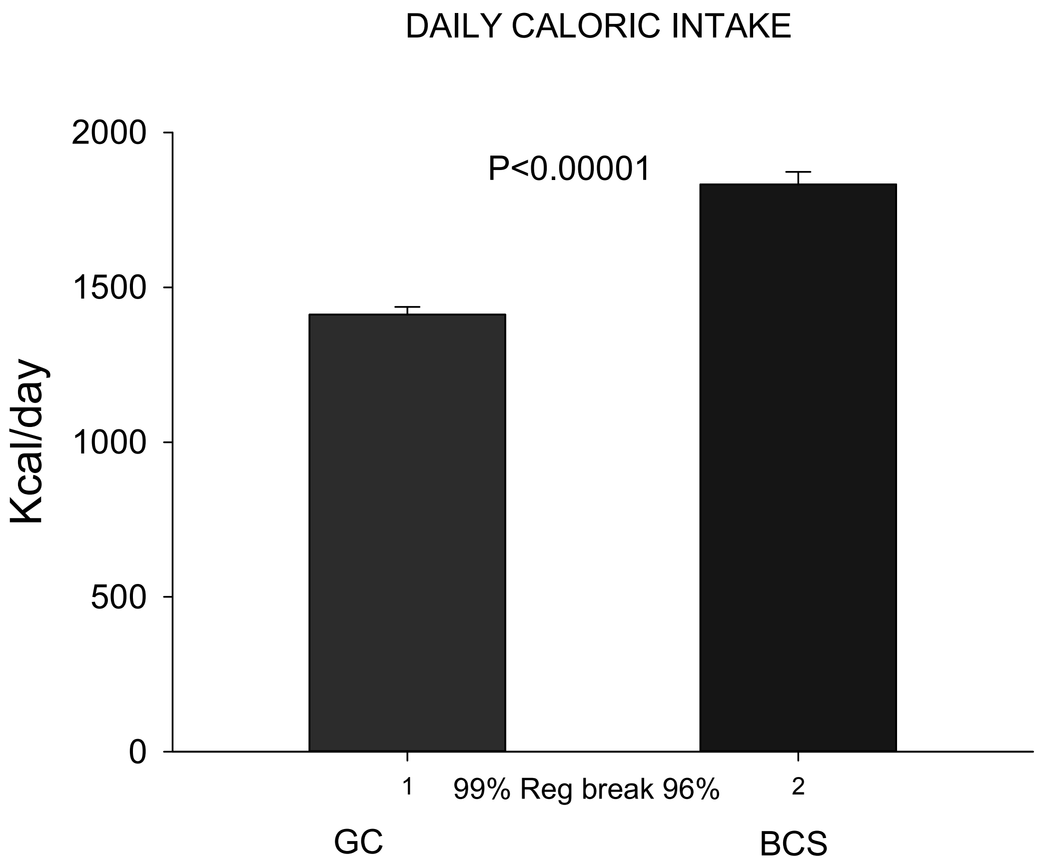


Figure 5: Smoking and alcohol consumption in two groups

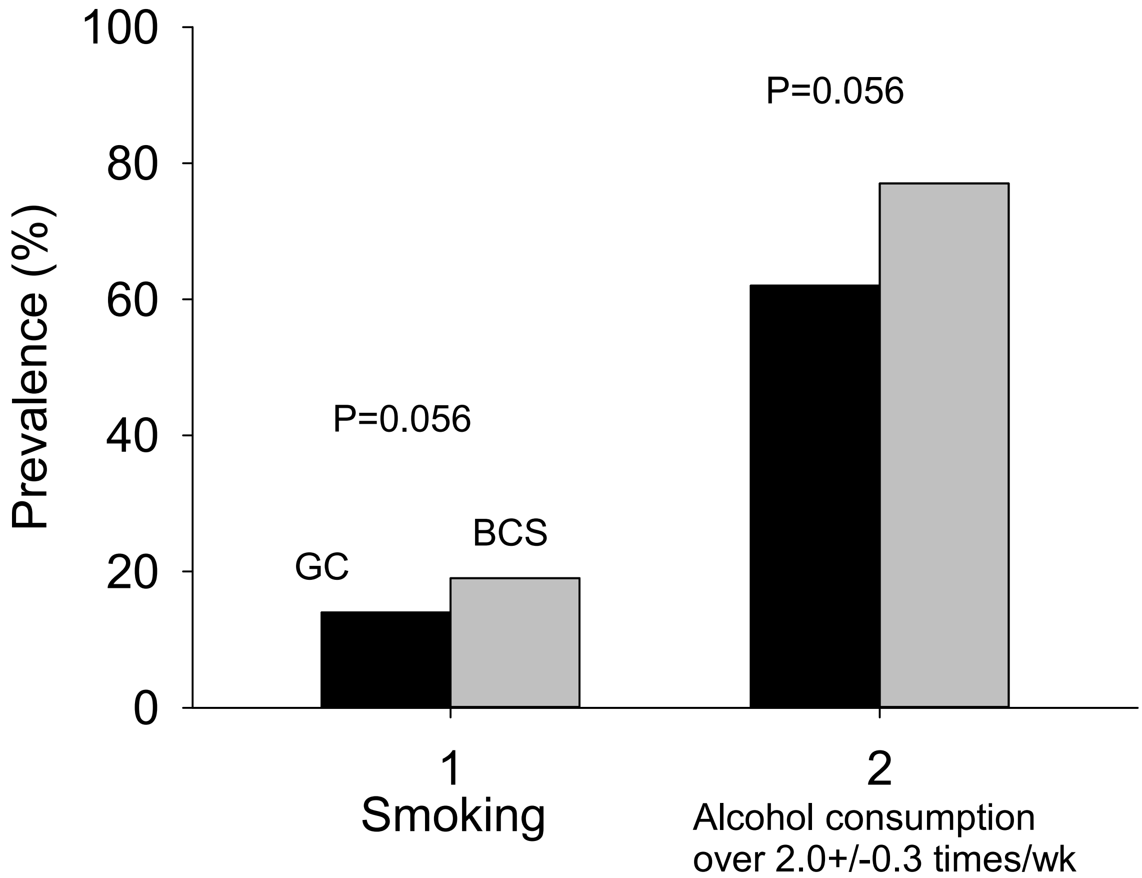


Figure 6: Olive oil consumption in two groups

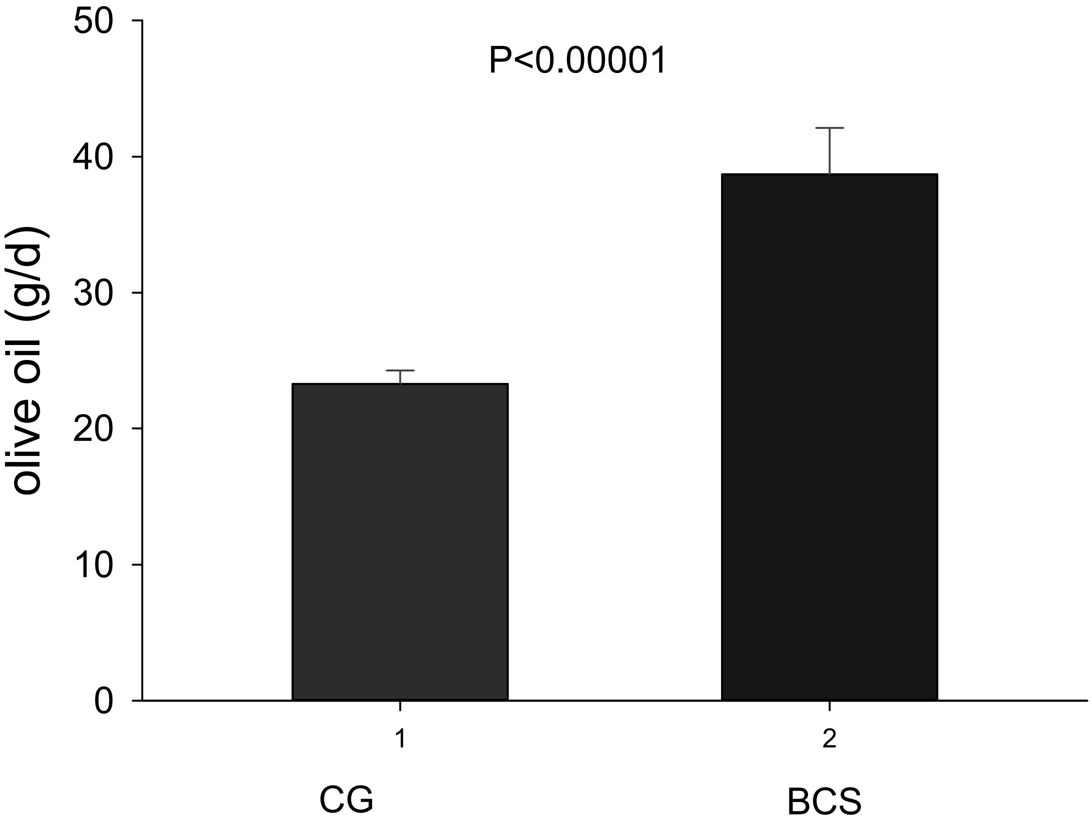


Figure 7: Junk score in two groups

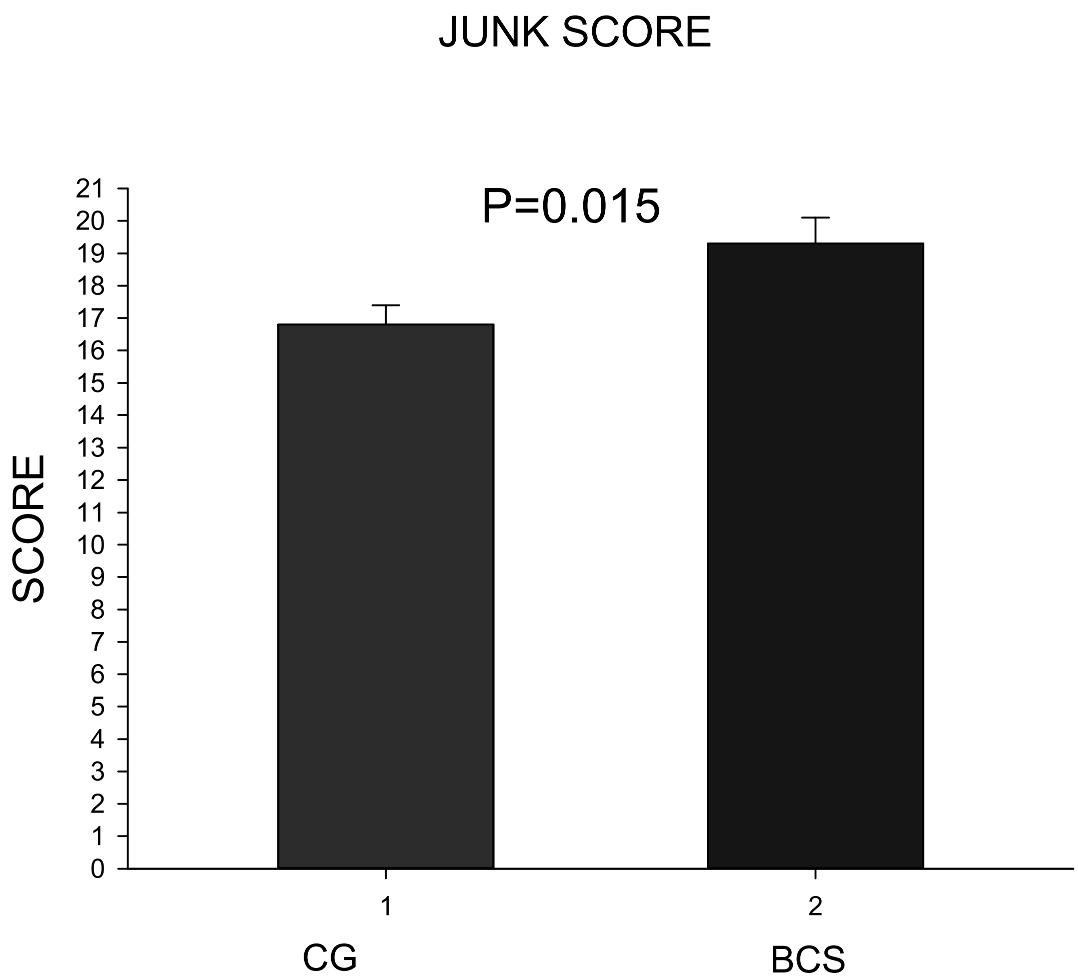


Figure 8: Legume intake in two groups

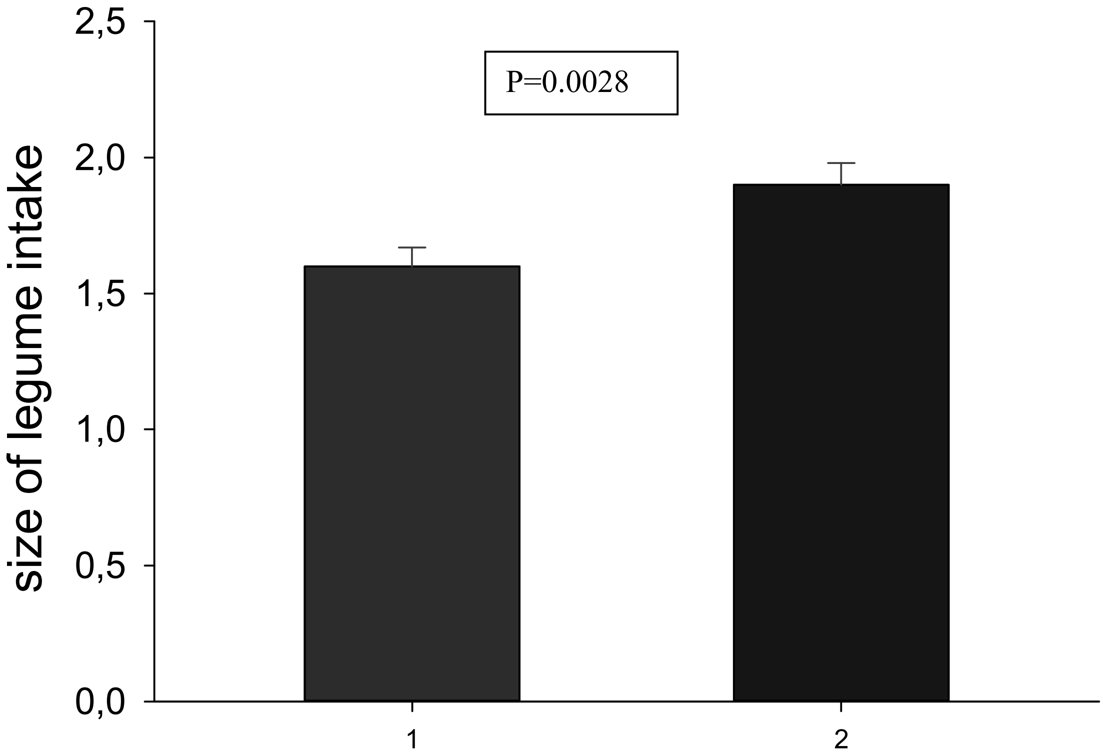


Figure 9: Fiber intake in two groups

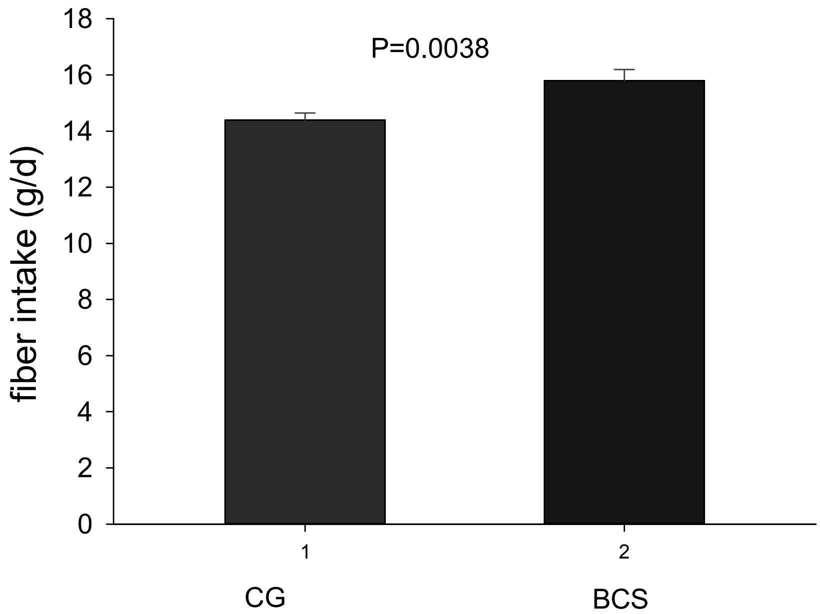
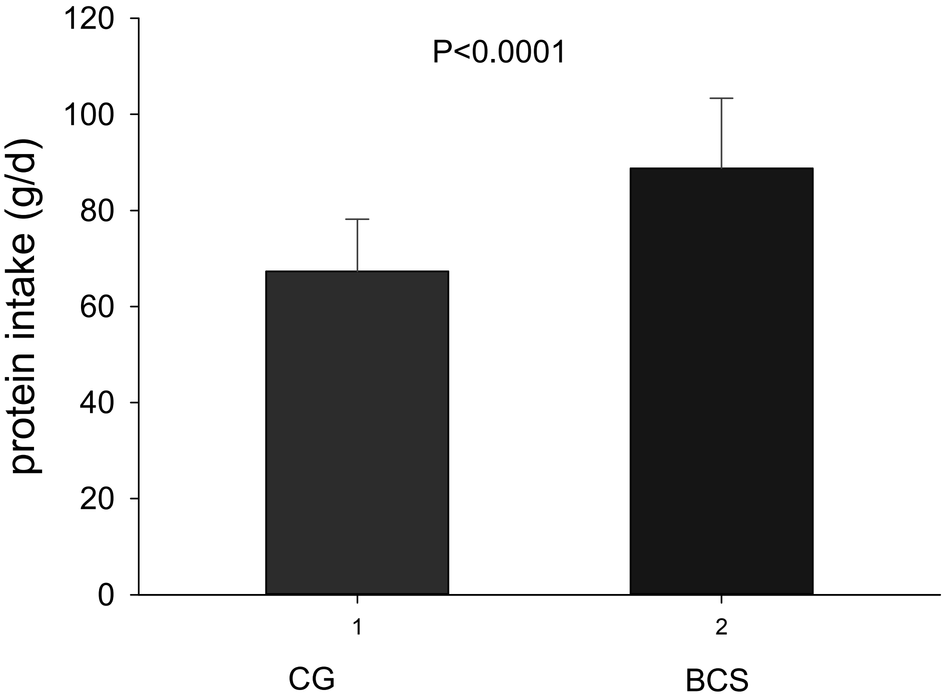


Figure 10: Protein intake in two groups



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