Somatotype and risk of breast cancer: a case-control study in Uruguay

Somatotipo de risco de câncer de mama: um estudo caso-controle no Uruguai

Abstract

According to the evidence, there is a need for more thorough assessment and quantification of body size and shape and the risk of breast cancer. Using the somatotype methodology, we carried out an original research in order to explore possible associations between body shape and the risk of breast cancer in Uruguayan women. With this objective, 254 recent breast cancer cases and 1,000 frequency-matched healthy controls were interviewed on menstrual and reproductive story, and a series of skinfolds, circumferences and diameters were measured specifically to calculate somatotype. A positive association with breast cancer was found for high endomorphy (Odds Ratio [OR] = 2.82, $p < 0.001$), mainly among premenopausal women (OR = 4.98, $p < 0.001$) and normoweight women (OR = 5.12, $p = 0.002$), whereas almost no differences were observed for mesomorphic and ectomorphic women. Analysis showed a high meso-endomorphic pattern in the study population. Further studies are needed to confirm the present results obtained in a country with high incidence of the disease.

Keywords: Anthropometry. Breast cancer. Epidemiology. Menopause. Somatotype.

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Resumo

Segundo as evidências, há uma necessidade mais profunda de avaliação e quantificação da dimensão e da forma corporal e o risco de câncer de mama (CM). Utilizando a metodologia do somatotipo, realizamos uma pesquisa original com o objetivo de explorar possíveis associações entre a forma corporal e o risco de CM nas mulheres uruguaias. Com essa finalidade, 254 casos recentes de CM e 1.000 controles emparelhados por freqüência foram entrevistadas sobre história menstrual e reprodutiva, e uma série de dobras cutâneas, circunferências e diâmetros foram medidas especificamente para se fazer o cálculo do somatotipo. Foi encontrada uma associação positiva com CM para forte endomorfismo (OR = 2.82, p < 0.001), especialmente nas mulheres pré-menopáusicas (OR = 4.98, p < 0.001) e com normopeso (OR = 5.12, p = 0.002); entretanto, não foram observadas diferenças para mesomorfismo e ectomorfismo. As análises apresentaram um elevado padrão meso-endomórfico na população estudada. São necessários novos estudos para confirmar os resultados presentes, obtidos em um país com elevada incidência da enfermidade.

Palavras-chave: Antropometria. Câncer de mama. Epidemiologia. Menopausa. Somatotype.

Introduction

Anthropometric measures have been included as potential risk factors for breast cancer (BC). Research in obesity has clearly demonstrated that it is a heterogeneous condition in terms of etiology and its association with health outcomes[1,2]. A woman's build, obesity, fat distribution, increased height and body mass index and weight gain have been found to increase risk in some studies but not in all of them[3]. Concerning this, menopausal status emerged as a key factor to analyze different subpopulations in view of the contrasting results obtained by epidemiologic research.

Some studies examined regional adiposity and BC risk[4-11]. A positive association of central adiposity with postmenopausal BC risk and also a weaker association for premenopausal women were found in most of these studies. Absence of association with anthropometric measures in premenopausal women was described in certain populations, like the Chinese[8,9]. More recently, waist-to-hip ratio was associated with an increased risk in pre-menopausal Nigerian[10] and Asian-American women[11] and also the fat-free mass has been found to be positively associated with the risk of BC in postmenopausal women[12].

A recent review on anthropometry and BC[3] recognized that more detailed, standardized, reliable and validated assessments of body size and shape are needed. Also, better classification according to fat localization is needed so that differences in fat deposition can be appropriately measured. Moreover, McTiernan[13] suggested the usefulness of case-control studies on anthropometric factors in racial and ethnic minorities, since these groups have not yet been sufficiently studied.

A somatotype is "a quantitative description of the present shape and composition of the human body"[14]. This method of physical classification was developed by W.H. Sheldon from the 1920's to 1950's[15] and was refined later[16]. A somatotype describes the human physique as a whole, which can

be broken down into three components presented and read in this order: endomorphy, mesomorphy and ectomorphy. These components differ between populations according to origin, age, and sex. Some patterns of familial correlations suggest the role of genetic factors in explaining variation in human physique[17], at least for mesomorphy[18]. The changes that occur in a somatotype happen during childhood to maturity. However, somatotypes can be altered through training and/or nutrition. An endomorphic somatotype characterizes the relative fatness of a person's body. The mesomorphic somatotype is characterized by musculo-skeletal size. Ectomorphy is characterized by relative linearity or slenderness and is derived from the ponderal index (height in cm divided by the cube root of weight in kg).

Originally, everyone's body shape was described by three numbers from 1 to 7, one for each of the three basic somatotypes, although longer scales are currently also used. The dominant somatotype of a subject is defined as a somatotype component rating at least 0.5 points higher than either of the other two component ratings. Ratings on each component up to 2.5 are considered low, 3 to 5 are moderate, 5.5 to 7 are high, and 7.5 and above are very high[14] . The highest value leads to the labeling of an individual, according to this prevailing component. The rating is phenotypical, based on the concept of geometrical size-dissociation and applicable to both genders from childhood to old age.

Examples of average somatotypes of non-athletic women are an elderly group in the Czech Republic [9] with 5.4 – 5.7 – 0.6, or a group of Belgian nursing professionals, with mean values of 5.0 – 4.0 – 2.0[20]. A specific chart (somatochart) is commonly used to give a visual expression of the quoted proportions. It has a central point whose values (4 – 4 – 4) represent a theoretical perfect balance among proportions.

According to international publications,[21] Uruguay is a country with a very high incidence of BC. In the past ten years the disease risk has been thoroughly studied from the dietary viewpoint[22-9] but not from the anthropometric standpoint yet. In almost all of the quoted hospital-based studies, which were performed at public institutions, BMI has not shown any association with BC risk and also a high prevalence of overweight and obesity was observed in the population samples studied (around 65%).

We are not aware of any previous epidemiologic study on BC reported in the literature on the use of somatotype methodology in order to analyze body shape and its possible association with BC. Taking into account the appropriate conditions for such epidemiologic research that Uruguayan women have, we decided to perform the present exploratory study.

Subjects and Methods

The authors carried out a hospital-based case-control study on anthropometry and BC during the period between June/2004 and August/2006. Based on an estimated institutional incidence of 125 BC cases per year, we projected to interview and measure, during a 2.5-year period, 1,800 women up to the age of 70 as a convenience sample, 300 of them with recently diagnosed BC and 1,500 healthy controls (5 per case), aged ± 5 years in relation to cases, living in Uruguay and attending the public healthcare system (about 40% of the adult population). In Uruguay this subpopulation involves mainly the lowest socioeconomic strata.

The Instituto de Radiología y Centro de Lucha Contra el Cáncer is a reference center for BC in Uruguay. Located at the Pereira Rossell Women's Hospital in Montevideo since the 1930's, it receives women coming from all over the country who receive care from the public health system. Currently, around 60 diagnostic mammograms in a predominantly asymptomatic population are performed daily.

During the study period, 254 new cases of BC up to the age of 70 were identified in the population screened, and enrolled in the study. Cases were women with new and

histologically diagnosed carcinomas – interviewed between 0 and 10 days after their diagnosis. Potential cases with ages over 70 were not taken into account, because of the lack of healthy controls to match them and also to reduce a possible recall bias. Eligibility criterion also accepted patients with a personal history of another cancer type (5% of all cases), provided they were in clinical cure at the moment of the interview. Their recruitment was performed in patients with mammogram BI-RADS 4 (suspicious of malignancy) and 5 (highly suspicious of cancer) lesions[30,31], and a positive cytological (on site) study, which was further histologically confirmed, according to its high correlation with histopathology[32]. Initially, no information on cancer staging was collected through the study period.

Since BC cases were interviewed and measured very early on, they had not yet experienced any post diagnostic or treatment-induced weight change. Although women do not formally participate in a screening program, cancers are usually diagnosed at early stages (ca. 15% carcinoma in situ). In the same time period, and in the same institution, 1,029 healthy women with a negative diagnostic mammogram (BIRADS categories 1 [completely negative]; 2 [only with findings not associated with pathology, e.g. benign calcifications and/or axillary lymphnodes])[0] performed on the same day of the interview, were randomly selected as controls. They were frequency-matched by age (± 5 years) to cases, being mandatory requirements for the controls not to be hospitalized at the moment of the interview and not having cancer. Most women aged under 30 were examined only with ultrasound, unless findings also required mammography, due to the high density of breasts at those ages. Normal aged controls were relatively infrequent in consulting at the Institute, and it is difficult to find completely normal mammograms in older women; therefore the ratio control/case was around 2:1 to 3:1, whereas among young and middle aged women that ratio was near 5:1. After excluding 27 women who had had cancer in the past (mostly uterine cervix) and 2 who refused the interview, a final number of 1,000 controls were recruited. Therefore, one thousand two hundred fifty four (1,254) women consulting for a mammography at the Instituto de Radiología y Centro de Lucha Contra el Cáncer in Montevideo were included in the study. Interviews and measurements were performed by only one nurse, who was blind to the objectives of the study, previously trained, and periodically supervised during the study period. All interviews were conducted in the hospital and performed face-to-face, and a written consent was obtained from every interviewed subject. People affiliated to the public health system are very cooperative; therefore a high participation is always expected. The research was approved by the ethical committee of the Hospital.

The questionnaire included the following sections:

- Sociodemographic variables;
- Menstrual and reproductive events (age at menarche, age at first live birth, number of children, months of breastfeeding, menopausal status (pre/post). Menopausal status was defined a priori: if according to the subject (aged >=45) menstruations had ceased at least for 6 months, excluding pregnancy, she was classified as postmenopausal;
- History of cancer in first and second degree relatives;
- Physical exercise (yes/no), frequency, duration and intensity and
- Self-reported weight at age 18. There was no question on hormonal replacement therapy, because it is not usually prescribed to postmenopausal women who belong to the studied subpopulation. The question about physical exercise referred to free-time activity, recreational or competitive, 5 years prior the interview. This assessment was performed only as an exploratory tool in the studied group, whose low income limits their time and access to sport institutions. The method was not validated.

Concerning anthropometry, the following measurements were taken:

- height (measured to the nearest centimeter)
- weight (at intervals of 0.100 kg)
- circumferences (in cm): (waist, hip, flexed and tensed arm, calf)
- skinfolds (in mm): tricipital, subscapular, supraspinal, calf)
- diameters (in mm): bicondyleal (femur) and bicondyleal (humerus).

Anthropometric equipment included a height scale and headboard, a weighing scale, a Vernier caliper, a flexible plastic measuring tape, and a skinfold caliper. The same mechanical scale was used along the whole study period, with a weekly calibration. Subjects were weighed wearing minimal clothing. For body measurements a plastic measuring tape at intervals of 0.5 cm (for circumferences), a Vernier caliper (for diameters) and a FatTrack Pro ® (Accufitness, Greenwood Village, CO, USA) digital caliper (for skinfolds) were used. Regarding these latter, if two consecutive measurements were similar, the value obtained was registered as valid. If both were different, a third one was taken and the median value was then registered. Measurements were performed according to Carter's Instruction Manual[33].

Somatotype

There are three extreme types:

- Extreme Endomorph: wide hips and narrow shoulders (pear-shaped), high fatness on the body, upper arms and thighs, quite slim wrists and ankles;
- Extreme Mesomorph: broad shoulders and relatively narrow hips (wedge-shaped), muscular body, strong forearms and thighs, very little body fat;
- Extreme Ectomorph: narrow shoulders, hips and chest, thin face, high forehead, thin legs and arms, very little muscle or fat.

Calculations of somatotype for each patient were done with specialized software[34]. The following measurements were taken into account: height, weight, four skinfolds (triceps, subscapular, supraspinal, and medial calf), two circumferences (tensed arm, calf), and two bone breadths (humerus, femur). Mean values of somatotype were calculated for all cases and all controls. Formulas applied to calculate somatotype are the following:

Endomorphy = - 0.7182 + 0.1451 (Σ) - 0.00068 (Σ^2) + 0.0000014 (Σ^3)

Mesomorphy = (0.858 HB + 0.601 FB +0.188 CAG + 0.161 CCG) - (0.131 H) + 4.5

Ectomorphy:

If HWR $\geq$ 40.75, then Ectomorphy = 0.732 HWR - 28.58

If HWR < 40.75 and > 38.25, then Ectomorphy = 0.463 HWR - 17.63

If HWR $\leq$ 38.25, then Ectomorphy = 0.1

where: Σ = (sum of triceps, subscapular and supraspinale skinfolds) multiplied by (170.18/height in cm); HB = humerus breadth; FB = femur breadth; CAG = corrected arm girth; CCG = corrected calf girth; H = height; HWR = height / cube root of weight.

CAG and CCG are the girths corrected for the triceps or calf skinfolds respectively as follows: CAG = flexed arm girth - triceps skinfold/10; CCG = maximal calf girth - calf skinfold/10.

Statistic analysis

Calculations of mean ± standard deviation for each variable were made. Based on the measurements done, the following calculations were made: Body Mass Index (BMI, kg/m2), BMI at age 18 (kg/m2), BMI difference (current-18 yrs), weight difference (id.) and waist-to-hip ratio. Somatotype variables were classified in tertiles, according to control distribution. Crude and adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI)s were calculated by unconditional logistic regression[35]. Potential confounders were included in the multivariate analysis. OR's were calculated including age, age at menarche, parity, age at first live birth, months of breastfeeding, time between menarche

and first delivery, use of oral contraceptives, BMI, BMI at age 18, physical exercise, menopausal status, and family history of BC. For analysis purposes, stratifications by menopausal status (pre-/post-) and by levels of body mass index (normoweight, overweight, obese) were also carried out. A P-value for trend was calculated for risk estimates using the chi-square test for linear trend. All calculations were performed with STATA software (Release 6, College Station, Texas, USA 1999).

Results

The general characteristics of the sample analyzed are presented in Table 1. At the moment of closing the entry of subjects' data to perform the current analysis (August/2006), some lack of age controls was observed. A very homogeneous population was described. Except for certain reproductive variables (age at first live birth, number of full-term pregnancies, and time of breastfeeding), education, urban/rural status, oral contraception, BMI, practice of physical exercise, menopausal status, and age at menarche were very similar.

Table 2 shows the anthropometric features of the study population. Whereas measured circumferences tended to be rather similar, skinfolds were significantly thicker among cases. Among diameters, only bicondyleal of humerus showed statistical differences, also larger among cases (p = 0.02). Estimated BMI at age 18 showed significant differences (p = 0.01), higher for cases. Of somatotype variables, only endomorphy displayed significant differences between cases and controls (p = 0.004), being higher for cancer cases. The average somatotype for the whole population was 6.6 – 5.6 – 0.7 (data not shown). According to these numbers, the global somatytype pattern is a strong meso-endomorphic one.

Table 3 shows crude and adjusted OR's for endomorphy, mesomorphy and ectomorphy. Considering both crude and adjusted OR's, a high endomorphy was positively associated with the risk of BC (OR = 1.49 and OR = 2.82 respectively). High mesomorphy tended to show a slight increase in risk (OR = 1.26 and OR = 1.47 respect.), albeit not significant. Ectomorphy displayed a lack of association with BC (OR = 0.92 and OR = 0.78 for crude and adjusted values, respectively).

When endomorphy was discriminated by menopausal status, some differences arose, as seen on Table 4. On one side, among pre-menopausal women, the calculated OR's for the highest tertiles of endomorphy were positively and significantly associated with the risk of BC, both crude and adjusted (OR = 1.97 and OR = 4.98, respect.). On the other hand, among postmenopausal women, only the adjusted OR's were strongly associated with BC (OR = 1.98, p-value for trend = 0.03). Nevertheless, a test for heterogeneity failed to demonstrate differences between both subgroups (p = 0.42, results not shown).

Finally, analyses stratifying data by BMI level (Table 5) showed that high endomorphy had a stronger association with risk of BC among normoweight women than among overweight and obese, for crude OR (OR = 5.26 vs. 1.65, respect.) and for adjusted OR's (OR = 5.12 vs. 2.06, respect.). In all cases, statistical trends were highly significant. Also here the test for heterogeneity did not demonstrate differences between both subsets (p = 0.25, results not shown). An additional likelihood ratio test for interaction performed to categories of endomorphy adjusted by BMI (dichotomized) indicated non significant differences (p = 0.14, results not shown).

Discussion

Our results show that certain body measurements are associated with BC risk in the population analyzed, despite menopausal status and BMI level. The somatotype approach enabled us somehow to quantify the proportions and shapes of all study women, as well as of each subset. To our knowledge, this is the first report on anthropometry and BC that uses this methodology. Cancer

Table 1 - General features of the study population (Uruguay, 2004-06): Sociodemographic, menstrual, reproductive and other selected variables of interest. Relative frequencies and p-value of differences between cases (n=254) and controls (n=1000).
Tabela 1 *– Características gerais da população estudada (Uruguai, 2004-06): Variáveis sociodemográficas, reprodutivas e outras variáveis selecionadas de interesse. Freqüências relativas e valor p das diferenças entre casos (n=254) e controles (n=1000).*

Variable		CASES	%	CONTROLS	%	p-value
Age (yrs)	<=34	20	7.9	79	7.9	
	35-39	18	7.1	91	9.1	
	40-44	33	13.0	161	16.1	
	45-49	42	16.5	175	17.5	
	50-54	36	14.2	145	14.5	
	55-59	33	13.0	151	15.1	
	60-64	37	14.6	118	11.8	
	>=65	35	13.8	80	8.0	0.12
Urban/rural Status	Urban	246	96.9	985	98.5	
	Rural	8	3.1	15	1.5	0.11
Education (yrs)	<=6	128	50.4	487	48.7	
	>=7	126	49.6	513	51.3	0.63
Menopausal status	Pre-	115	45.3	463	46.3	
	Post-	139	54.7	537	53.7	0.77
Age at menarche	<=12	133	52.4	495	49.5	
	>=13	121	47.6	505	50.5	0.41
Age at first live birth	Nulliparous	27	10.6	73	7.3	
	13- 21	90	35.4	492	49.2	
	>=22	137	53.9	435	43.5	0.0003
Number of Full-term Pregnancies	Nulliparous	27	10.6	73	7.3	
	1- 2	124	48.8	445	44.5	
	>=3	103	40.6	482	48.2	0.04
Breastfeeding (months)	No	55	21.7	152	15.2	
	1-18	114	44.9	477	47.7	
	>=19	85	33.5	371	37.1	0.04
Fam.history of BC	No	180	70.9	762	76.2	
	Yes	74	29.1	238	23.8	0.08
Oral contraception (no/yes)	No	109	42.9	396	39.6	
	Yes	145	57.1	604	60.4	0.34
Body Mass Index	NW	91	35.8	328	32.8	
	OW	77	30.3	365	36.5	
	OB	86	33.9	307	30.7	0.18
Physical exercise (no/yes)	No	163	64.2	623	62.3	
	Yes	91	35.8	377	37.7	0.58
Physical exercise (times/ week)	No	163	64.2	623	62.3	
	1-3	26	10.2	133	13.3	
	>=4	65	25.6	244	24.4	0.42
Physical exercise (minutes/ week)	No	163	64.2	623	62.3	
	<=240	40	15.7	204	20.4	
	>240	51	20.1	173	17.3	0.20
Total patients	254	100.0	1000	100.0		

Abbreviations: NW=Normoweight (<=24.99 kg/m^2); OW=Overweight (25.0 – 29.99 kg/m^2); OB=Obesity (>30 kg/m^2) / *Abreviaturas: NW=Normopeso (<=24,99 kg/m^2) ; OW=sobrepeso (25,0 – 29,99 kg/m^2); OB=Obesidade (>30 kg/m^2).*

Table 2 - Anthropometric features of the study population. (Uruguay, 2004-06): Mean values ± Standard Deviation of each measurement and p-value of differences between cases (n=254) and controls (n=1000).

Tabela 2 – *Características antropométricas da população estudada. (Uruguai, 2004-06): valores medianos ± desvio padrão de cada medição e valor p das diferenças entre casos (n=254) e controles (n=1000).*

Variable	CASES	CONTROLS	
	Mean ± SD	Mean ± SD	p-value
Height (cm)	157.26 ± 5.92	157.90 ± 6.20	0.14
Weight (kg)	70.00 ± 16.20	69.60 ± 13.68	0.69
Weight at age 18 (kg)	54.92 ± 9.68	53.95 ± 8.93	0.13
CIRCUMFERENCES (cm)			
Waist	93.21 ± 14.12	92.33 ± 12.03	0.32
Hip	103.40 ± 13.11	103.03 ± 11.39	0.66
Tensed arm	32.28 ± 4.56	32.09 ± 3.94	0.50
Calf	37.43 ± 4.44	37.37 ± 4.66	0.85
SKINFOLDS (mm)			
Tricipital	28.16 ± 11.00	25.64 ± 9.91	0.0004
Subscapular	28.76 ± 12.58	26.70 ± 10.44	0.007
Supraspinal	22.25 ± 10.81	20.46 ± 9.43	0.009
Calf	36.95 ± 12.88	32.48 ± 10.50	<0.0001
DIAMETERS (mm)			
Bicondyleal (elbow)	62.37 ± 5.36	61.58 ± 4.87	0.02
Bicondyleal (knee)	90.18 ± 9.76	90.16 ± 8.69	0.97
CALCULATIONS			
BMI (kg/m2)	28.31 ± 6.36	27.94 ± 5.46	0.36
BMI at age 18 (kg/m2)	22.22 ± 3.79	21.63 ± 3.34	0.01
Waist/hip ratio	0.899 ± 0.055	0.895 ± 0.051	0.22
Endomorphy	6.91 ± 1.96	6.54 ± 1.81	0.004
Mesomorphy	5.65 ± 2.00	5.56 ± 1.79	0.48
Ectomorphy	0.79 ± 0.99	0.75 ± 0.93	0.55

Abbreviation: SD = Standard Deviation

cases displayed a higher endomorphy than healthy controls in all analyses, while mesomorphy did not reach significance and ectomorphy was almost similar for cases and controls. Endomorphy displayed strong positive associations with BC risk after crude and adjusted analyses, mainly for the whole sample (OR = 1.56 vs. 2.86), for premenopausal women (OR = 1.98 vs. 5.08), and for normoweight ones (OR = 5.27 vs. 5.34), although formal tests for interaction failed to demonstrate heterogeneity in these two latter situations. Taking into account, on one hand, that mean weight values for cases and controls were not different and, on the other hand, that the selected skinfolds were notably higher among cases, there is evidence for a different distribution of their weight, particularly taking into consideration the adipose component. Despite the significance of OR's, trends of endomorphy showed a dose-response pattern in all analyses, which reinforces its possible role as a risk factor for BC.

Table 3 - Crude and adjusted OR's of somatotype components. Estimates according to division of each component into tertiles.
Tabela 3 *– OR's brutas e ajustadas de componentes do somatotipo. Estimativas segundo divisão de cada componente em tercis.*

			ENDOMORPHY			
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	73/333	<= 6.0	1.00	-	1.00	-
MID	76/346	6.1 -7.4	1.00	0.70 – 1.43	1.38	0.92 – 2.08
HIGH	105/321	>= 7.5	1.49	1.07 – 2.09	2.82	1.70 – 4.70
Trend			p = 0.02		p < 0.001	
			MESOMORPHY			
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	86/335	<= 4.6	1.00	-	1.00	-
MID	69/333	4.7 -6.1	0.81	0.57 – 1.15	0.88	0.58 – 1.33
HIGH	99/332	>= 6.2	1.16	0.84 – 1.61	1.47	0.87 – 2.49
Trend			p = 0.93		p = 0.12	
			ECTOMORPHY			
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	116/448	0.1	1.00	-	1.00	-
MID	68/259	0.2 -0.9	1.01	0.72 – 1.42	0.89	0.56 – 1.43
HIGH	70/293	>= 1.0	0.92	0.66 – 1.28	0.78	0.39 – 1.56
Trend			p = 0.66		p = 0.48	

Adjustment terms: age (continuous), education (continuous), urban/rural status (urban/rural), age at menarche (continuous), number of live births (continuous), age at first delivery (continuous), months of breastfeeding (continuous), years between menarche and first delivery (continuous), menopausal status (pre-/post-), family history of breast cancer (yes/no), use of oral contraception (yes/no), weight at age 18 (continuous), physical exercise (yes/no), body mass index (categorical, normoweight, overweight, obese). P-values in Table refer to linear trends of estimates.

A greater upper or central body fat distribution has been reported mainly as associated with multiple hormonal and metabolic changes including insulin resistance, hyperinsulinemia, decrease in SHBG (sex hormone-binding globulin) levels, increase in androgen levels, and the conversion of androgen to estrogen in adipose tissue[36-38]. Therefore, women having this pattern associated with increased risk for diabetes mellitus, hypertension and cardiovascular disease may have theoretically a higher risk for BC than women whose fat is mainly distributed over hips, buttocks, and lower extremities. Since BC is a multifactorial disease, western lifestyle may act on the incidence of BC through an influence on body fat distribution and resulting changes in sex steroid availability[39]. In our report, on the contrary, a high endomorphy (rather similar to the gynoid-type obesity) was found as positively associated with the risk of BC, despite menopausal status. Regarding this, a higher aromatase activity was also described almost two decades ago in these body regions[40] and it could be a plausible explanation for our current findings. We also found similar waist-to-hip ratios, not suggesting the existence of central-type obesity. These somehow unexpected results enable us to think that ethnical factors should be taken into ac-

Table 4 - Crude and adjusted OR's of Endomorphy, stratified by menopausal status. Estimates according to division of each status into tertiles.
Tabela 4 *– OR's brutas e ajustadas de endomorfia, estratificadas por condição menopausal. Estimativas segundo divisão de cada condição em tercis.*

	PREMENOPAUSAL WOMEN					
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	35/186	<= 6.0	1.00	-	1.00	-
MID	33/150	6.1 -7.4	1.17	0.69 – 1.97	1.72	0.96 – 3.08
HIGH	47/127	>= 7.5	1.97	1.20 – 3.22	4.98	2.25 – 11.0
Trend			p = 0.007		p < 0.001	
	POSTMENOPAUSAL WOMEN					
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	38/147	<= 6.0	1.00	-	1.00	-
MID	43/196	6.1 -7.4	0.85	0.52 – 1.38	1.16	0.65 – 2.06
HIGH	58/194	>= 7.5	1.16	0.73 – 1.84	1.98	1.00 – 3.90
Trend			p = 0.46		p = 0.03	

Adjustment included age (continuous), age at menarche (continuous), parity (continuous), age at first live birth (continuous), months of breastfeeding (continuous), years between menarche and first delivery (continuous), BMI (continuous), BMI at age 18 (continuous), use of oral contraceptives (yes/no) and family history of BC (yes/no). For postmenopausal, age at menopause (continuous) was included as a regression term. P-values in Table refer to linear trends of estimates.

count, in view of the different origins that Uruguayan women have when compared with Americans, Scandinavians or others from first world countries.

The inclusion of BMI as an adjustment term and the high OR's found also among women who are normoweight according to BMI criteria lead us to think about the potential importance of body shape, in particular based on fat and muscle distribution, regarding the risk of BC. A gynoid-type obesity should be carefully considered from the clinical viewpoint, since it appears as a likely drawback for prevention and/or treatment of BC, considering that the anatomic site can imply in a non desirable excess of hormonal synthesis. Regarding women's typical hormone-related cancers (breast, endometrium, ovary), this relatively simple technique deserves to be explored in broader population groups and also for the patient follow-up.

As other case-control studies, our work has limitations and strengths. A major limitation is related to the current sample size; it would be desirable to analyze a larger one, in order to have enough statistical power for certain results, in particular in some subsets. Another limitation is the impossibility to compare our results with those of another similar report, a common issue in initial studies. In fact, somatotype is an analysis technique that has been almost exclusively used for fitness and athletic assessment, but infrequently within the medical field. Historically it has been mainly related to serum lipids and cardiovascular risk[41-45], as well as to obesity[46,47] and scarcely used in cancer research[48,49]. Recent research showed a great potential for sophisticated technology to perform precise somatotype classification[50]. Thus, manual procedures such as those utilized here probably have greater measurement errors at the individual level. Nevertheless, they are still useful for population studies.

On the other hand, both cases and controls belong to a very homogeneous base subpopulation: they were not only matched by age, but they also proceeded from the

Table 5 - Crude and adjusted OR's of Endomorphy, stratified by Body Mass Index levels (*). Estimates according to division of endomorphy into tertiles.
Tabela 5 *– OR's brutas e ajustadas de endomorfia, estratificadas por níveis de índice de massa corporal (*).Estimativas segundo divisão de endomorfia em tercis.*

			NORMOWEIGHT			
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	58/254	<= 6.0	1.00	-	1.00	-
MID	69/27	6.1 -7.4	1.71	1.01 – 2.91	1.90	1.09 – 3.31
HIGH	5/6	>= 7.5	5.26	1.55 – 17.8	5.12	1.38 – 19.0
Trend			p = 0.002		p = 0.002	
			OVERWEIGHT-OBESE			
	Cases/ controls	Cutpoints	Crude OR	(95% CI)	Adjusted OR	(95%CI)
LOW	15/79	<= 6.0	1.00	-	1.00	-
MID	49/277	6.1 -7.4	0.93	0.50 – 1.75	1.12	0.58 – 2.16
HIGH	99/316	>= 7.5	1.65	0.94 – 2.99	2.06	1.09 – 3.90
Trend			p = 0.006		p = 0.002	

Adjustment terms: age (continuous), education (continuous), urban/rural status (urban/rural), age at menarche (continuous), number of live births (continuous), age at first delivery (continuous), months of breastfeeding (continuous), years between menarche and first delivery (continuous), menopausal status (pre-/post-), family history of breast cancer (yes/no), use of oral contraception (yes/no), weight at age 18 (continuous) and physical exercise (yes/no). P-values in Table refer to linear trends of estimates.
(*) Normoweight <=24.99 kg/m^2; Overweight-obese >=25.0 kg/m^2 / *(*) Normopeso <=24,99 kg/m^2; sobrepeso-obeso >=25,0 kg/m^2*

same healthcare system and they exhibited similarities concerning most sociodemographic and some reproductive variables. To be quoted also among the strengths, we selected as controls mostly women with normal breasts, not only without cancer; therefore, if benign breast diseases had any association with the analyzed anthropometric items, we attempted to reduce their possibility of biasing results. In order to reduce a possible recall bias, eligible patients were up to age 70. Finally, this is a very cooperative population; therefore, high participation was achieved. Although it is not possible to avoid any bias completely, we think that results were not chance findings. Still, we need caution in the interpretation of results, since generalizing is limited due to population features: they have mid-to-low educational level and belong to low socioeconomic classes of a developing country.

In conclusion, we examined various anthropometric measures using a novel approach in an effort to better describe possible associations of body shape with the risk of BC. Somatotype analysis revealed that cases were more endomorphic than controls. High endomorphy was positively and significantly associated with BC despite menopausal status and BMI level. It should also be taken into account that the study population belongs to a subset of a BC high-risk country like Uruguay, mainly with Hispanic and Latin European origins; therefore, we cannot extrapolate our results to elsewhere. Our study is still ongoing, and new analyses of cancer staging in a larger sample, as well as with other women of different origins are needed to confirm the suggested trends. Indeed, this is a task for the close future.

AUTHORS DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

No relationships, neither financial nor of other nature, to disclose.

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