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ORIGINAL PAPER

Body size and breast cancer in a black population—The Barbados National Cancer Study

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Abstract
Objective To evaluate the relationship between body size and incident breast cancer in an African-origin Caribbean population.
Methods This investigation is based on 222 incident breast cancer cases and 454 controls from the Barbados National Cancer Study (BNCS) in whom body size variables that included height, weight, body-mass index (BMI), waist and hip circumferences (WC, HC), and waist−hip ratio (WHR) were compared. Multivariate-adjusted logistic regression analyses were performed and the findings are presented as odds ratios (ORs) with 95% confidence intervals (CI).
Results Although 33% of cases and 39% of controls were obese (BMI $\geq$ 30 kg/m^2), BMI was not found to be a significant predictor of breast cancer in the multivariate analyses. Tall stature increased risk among women $\geq$50 years (OR = 2.16, 95% CI (1.02, 4.58)), and a dual effect with age was suggested for both WC and WHR (decreased risk for those aged $\leq$50 years; increased risk among those $\geq$50 years).
Conclusions Body size appears to influence the risk of breast cancer in this population of African origin. The BNCS data suggest that a few, but not all body size factors play a role in breast cancer risk, and that age may affect these relationships.

Keywords Height · Weight · Body circumferences · Breast cancer · African ancestry

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Introduction

It has long been postulated that body size may play a key role in the development of breast cancer. Indicators such as height [1–5], weight [2, 4–7], body mass index (BMI) [1, 8, 9], waist circumference (WC) [3, 6, 9, 10], waist–hip ratio (WHR), [3, 9, 11, 12] and weight changes [2, 6, 9, 13] have all been implicated as influencing breast cancer risk. The role of body size in breast cancer development has been found to interact with menopausal status. For example, increased weight/BMI may confer a decreased breast cancer risk in premenopausal women, yet increase risk in postmenopausal women; additionally, higher WC/WHR values may be associated with increased risk in postmenopausal women but are not related to breast cancer in those who are premenopausal [3]. These findings have mainly been derived from studies involving primarily European-origin women. Questions remain, however, as to whether similar risk profiles are appropriate for women of African origin. For example, if the prevalence of obesity is higher in African-American compared with White-American women, one might expect premenopausal African-American women to have a lower incidence of breast cancer and postmenopausal African-American women to have higher rates than their White-American counterparts [12]. This is not the case, however, as incidence and mortality rates among premenopausal African-American women are twice those found in White-American women and similar rates are reported among postmenopausal African-American and White-American women. The purpose of this investigation is to evaluate the relationship between body size factors and breast cancer in a westernized population of predominantly African-origin, which shares a common ancestry with African-Americans.

Materials and methods

The Barbados National Cancer Study (BNCS) is a population-based case–control study designed to evaluate risk factors for incident breast and prostate cancer in the predominantly African population of Barbados, West Indies. It was funded by the National Human Genome Research Institute (NHGRI), with contribution from the Office for Minority Health. The organizational structure of the project included a Coordinating Center (Stony Brook University, Stony Brook, NY), a Clinical Center (Ministry of Health, Bridgetown, Barbados, West Indies, and University of the West Indies, Barbados, West Indies), a Local Laboratory Center (University of the West Indies, Barbados, West Indies), a NHGRI Center (Bethesda, MD), and a Gene Discovery Center (Translational Genomics (TGen) Research Institute, Phoenix, AZ).

Cases were identified through the only Pathology Department on the island, located at the Queen Elizabeth Hospital, and included all histologically confirmed incident breast cancers between July, 2002 and March, 2006. A national database provided by the Barbados Statistical Services was used to randomly select controls. Eligibility criteria required all controls to be Barbadian citizens, at least 21 years of age and free of cancer at the time of the study examination. Breast cancer cases were frequency matched to controls at a 2:1 ratio and by 5-year age groups. Participation rates were 80 and 82% (among those eligible) among cases and controls, respectively, with the main reasons for non-participation being death, illness/disability, leaving the island, and refusal. Informed consent was obtained from all the BNCS participants and the study protocols conformed to the Declaration of Helsinki.

The study visit included a comprehensive nurse-administered interview, anthropometric and other measurements, and a clinical examination by one of the study's physicians. The BNCS protocol has been previously described in detail [14]. In brief, questionnaire items included demographic and lifestyle factors, a thorough gynecologic and medical history, and a complete family history of cancer. Strict guidelines were used to assess body size. Participants were asked to remove shoes and all excess clothing before any measurements were taken. Height was determined using a metric rule attached to a wall and a right-angled wooden block; weight was assessed using a beam balance scale, and waist and hip circumferences were obtained using flexible steel tapes. Waist circumference (WC) was measured at the maximum circumference between the lower ribs and the hip, usually around the area of the navel and hip circumference (HC) was determined at the level of greatest protrusion of the buttocks. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters and waist–hip ratio (WHR) as the WC divided by the HC.

A complete weight history from adolescence through adulthood was also obtained by nurse-interview, including weight data at 15, 20, and 40 years of age, as well as at a time point 5 years prior to the participants' reference date (a date corresponding to the date of diagnosis in the cases and a similar date in the matched controls). These data were collected after the beginning of the study. The protocol also included a comprehensive qualitative food frequency questionnaire and venipuncture for HbA1c and genetic variant testing. Mammograms were offered to all non-pregnant controls who did not have one within the previous year.

Statistical analyses

Chi-square statistics (for categorical variables) and *t*-tests (for continuous variables) were used to evaluate differences in body size factors between cases and controls. Body size variables were divided into clinically meaningful cut points and stratified by age (which was used as a proxy for menopausal status). WHO standards were used to define cutoffs for BMI and WHR, whereas quintile cutpoints were used for height, weight, and body circumferences. Values above the upper quintile were considered high, those below the lowest quintile were classified as low, and all others were defined as intermediate. Multivariate logistic regression analyses were performed and adjusted for age at the study visit, use of hormone replacement therapy (HRT), parity, family history of breast cancer, history of benign breast disease, age at first pregnancy, age at menarche, physical activity, and other body size variables. Results are presented as odds ratios (ORs) and 95% confidence intervals (CI), and analyses were conducted using the SAS statistical software package (Cary, NC) [15].

Results

The BNCS included 241 incident breast cancer cases and 481 female controls. Of those, 94% self-reported their race as African-Barbadian, resulting in 222 cases and 454 controls of African descent with mean (SD) ages of 57 (14.3) and 56 (14.1) years, respectively. Due to the small number of other ethnicities, this investigation is based on African-Barbadian participants only. Additional details including demographic and other factors relating to the BNCS cases and controls are presented in detail elsewhere [14].

Table 1 indicates that cases were generally taller than controls (mean (SD): 161.8 (6.1) vs. 160.8 (6.5) cm, $P = 0.04$), and their HC, on average, was 2 cm smaller than that of controls ($P = 0.03$). While cases weighed less than controls at their study visit, this finding is likely due to treatment and disease, as both groups had similar weights 5 years prior to the reference date (159.9 vs. 161.0 lbs, $P = 0.79$). Women with breast cancer tended to be heavier during adolescence (15 years of age), yet the 5-pound difference in weight at this age was only marginally significant ($P = 0.10$). This may be due, however, to the modest sample size of cases and controls with available weight history data. Weight at ages 20 and 40 years did not differ between cases and controls. Additional analyses indicated that there were no statistically significant differences in weight changes between cases and controls from 15, 20, and 40 years of age, respectively, until the reference date.

The data from Table 1 also indicate that obesity rates are high in Barbados, with more than one-third of cases and controls having a BMI ≥ 30 kg/m^2 and over one-half having a WC > 88 cm. Although observed rates of obesity as measured by BMI and WC were somewhat higher in the controls, the differences were not statistically significant, regardless of which measurement was used to define obesity.

The distribution of height stratified by age is presented in Table 2. The findings indicate that tallness is associated with breast cancer risk in older women (≥50 years) (OR = 2.16 (1.02, 4.58)) but not among their younger (≤50 years) counterparts. Overall, without stratification by age, a positive association was present between breast cancer and height (P-trend = 0.05) with women in the highest quintile being at greatest risk (OR = 1.94 (1.04, 3.65)).

The distribution of other body size factors stratified by age is presented in Table 3. In the multivariate adjusted models, neither current weight nor BMI were found to be associated with breast cancer risk, regardless of age. However, a possible dual effect was noted for two measures of central adiposity. Higher values of WC and WHR tended to be protective in women younger than 50 years

Table 1 Distribution of potential breast cancer risk factors related to body size among African-Barbadian women

Factors	Cases ($n = 222$) Mean ± SD (median)	Controls ($n = 454$) Mean ± SD (median)	P-value*
Body size			
Height (cm)[a]	161.8 ± 6.1 (162.0)	160.8 ± 6.5 (161.0)	0.04
Weight at age 15 years (lb)[b]	117.3 ± 20.6 (113.5)	112.0 ± 21.4 (110.0)	0.10
Weight at age 20 years (lb)[b]	126.8 ± 22.7 (120.0)	128.0 ± 23.3 (123.0)	0.69
Weight at age 40 years (lb)[b]	156.6 ± 32.4 (151.5)	159.3 ± 32.4 (153.5)	0.52
Weight 5 years prior to RD (lb)[b]	159.9 ± 36.1 (155.0)	161.0 ± 34.8 (155.0)	0.79
Current weight (lb)[a]	158.3 ± 34.9 (153.0)	165.6 ± 37.0 (161.0)	0.01
Body mass index (BMI) (kg/m^2)[a]	27.4 ± 5.8 (26.7)	29.1 ± 6.2 (28.6)	0.001
Waist circumference (WC) (cm)[a]	90.2 ± 12.6 (90.0)	91.4 ± 12.9 (91.0)	0.24
Hip circumference (HC) (cm)[a]	105.7 ± 11.3 (104.0)	107.8 ± 12.5 (106.0)	0.03
Waist–hip ratio (WHR)[a]	0.85 ± 0.08 (0.86)	0.85 ± 0.07 (0.85)	0.30
Obese (%)			
BMI ≥ 30 kg/m^2	33.3	39.2	0.14
WC > 88 cm	53.2	59.3	0.13
WHR > 0.8	73.5	73.4	0.97

RD reference date

* Based on t-tests for continuous variables and χ^2 tests for categorical variables

[a] Measurements taken during study visit

[b] Sample sizes: at age 15 (70 cases, 121 controls), at age 20 (88 cases, 173 controls), at age 40 (88 cases, 186 controls), at 5 years prior to RD (114 cases, 240 controls)

Table 2 Distribution of height by age

Height (cm)	Cases N (%)	Controls N (%)	Multivariate-adjusted OR (95% CI)[a]
<50 years			
<156	7 (91)	19 (11.5)	1.00
156 to <167	50 (64.9)	105 (63.6)	1.75 (0.54, 5.64)
≥167	20 (26.0)	41 (24.8)	1.36 (0.37, 4.96)
≥50 years			
<156	25 (17.4)	77 (26.7)	1.00
156 to < 167	89 (61.8)	161 (55.9)	1.67 (0.91, 3.08)
≥167	30 (20.8)	50 (17.4)	2.16 (1.02, 4.58)*

* $P < 0.05$ from logistic regression

[a] Multivariate analyses adjusted for current age, HRT, parity, family hx of BC, hx of benign breast disease, age at first pregnancy, age at menarche, physical activity, waist and hip circumference

and increased risk in older women. Among those ≥50 years, the OR was 2.98 (95% CI 0.91, 9.71) for WC ≥ 101 cm compared to 0.45 (0.10, 2.12) in women <50 years in the same WC strata. A separate sub-analysis among older women who never used HRT ($n = 106$ cases, $n = 209$ controls) showed even stronger statistically significant findings (OR = 4.08 (1.14, 14.64)). Although tests for trend did not achieve statistical significance for WC among women <50 years, likely due to the reduced sample size in this group, the risk increased with higher WC measurements in the older age group (P trend = 0.04). Tests for interaction also indicated a significant age by WC interaction ($P = 0.01$), thus supporting a possible dual effect by age. A similar pattern was noted for WHR. The ORs for WHR > 0.85 were 2.17 and 0.86 for older and younger women, respectively. The P-value for trend was 0.02 among women ≥50 years and an age by WHR interaction was noted ($P = 0.01$).

Discussion

A variety of body size variables including height, weight, weight change, and abdominal/hip circumferences have been suggested as being influential in the development of breast cancer. In the BNCS, a population of African-Barbadian women with high rates of obesity, increased height was found to be positively associated with breast cancer risk, whereas weight status during adulthood did not

Table 3 Distribution of body size factors by age

Body size factors	Age < 50 years			Age ≥ 50 years		
	Cases N (%)	Controls N (%)	Multivariate-adjusted[a] OR (95% CI)	Cases N (%)	Controls N (%)	Multivariate-adjusted[a] OR (95% CI)
Current weight (lb)						
<132	16 (20.8)	17 (10.3)	1.00	40 (28.2)	56 (19.5)	1.00
132 to <192	48 (62.3)	108 (65.4)	0.75 (0.28, 1.96)	78 (54.9)	173 (60.3)	0.57 (0.31, 1.06)
≥192	13 (16.9)	40 (24.2)	0.38 (0.12, 1.22)	24 (16.9)	58 (20.2)	0.59 (0.28, 1.25)
BMI (kg/m^2)						
<25	33 (42.9)	43 (26.1)	1.00	51 (35.9)	80 (28.0)	1.00
25 to <30	20 (26.0)	55 (33.3)	0.46 (0.20, 1.08)	42 (29.6)	96 (33.6)	0.67 (0.36, 1.24)
≥30	24 (31.2)	67 (40.6)	0.44 (0.19, 1.01)	49 (34.5)	110 (38.5)	0.70 (0.38, 1.28)
Waist circumference (cm)						
<80	27 (35.5)	34 (20.6)	1.00	18 (12.5)	34 (11.8)	1.00
80 to <101	41 (54.0)	104 (63.0)	0.70 (0.27, 1.80)	88 (61.1)	184 (64.1)	1.35 (0.57, 3.18)
≥101	8 (10.5)	27 (16.4)	0.45 (0.10, 2.12)	38 (26.4)	69 (24.0)	2.98 (0.91, 9.71)
Hip circumference (cm)						
<97	13 (17.1)	18 (10.9)	1.00	30 (21.0)	51 (17.8)	1.00
97 to <116	51 (67.1)	108 (65.4)	1.81 (0.62, 5.29)	84 (58.7)	168 (58.7)	0.95 (0.46, 1.97)
≥116	12 (15.8)	39 (23.6)	1.14 (0.27, 4.90)	29 (20.3)	67 (23.4)	0.76 (0.26, 2.24)
WHR						
<0.8	38 (50.0)	68 (41.2)	1.00	16 (11.2)	45 (15.7)	1.00
0.8 to <0.85	22 (29.0)	48 (29.1)	1.08 (0.48, 2.42)	29 (20.3)	73 (25.5)	1.19 (0.52, 2.71)
≥0.85	16 (21.0)	49 (29.7)	0.86 (0.37, 1.98)	98 (68.5)	168 (58.7)	2.17 (1.02, 4.60)*

* $P < 0.05$ from logistic regression

[a] Multivariate analyses adjusted for current age, HRT, parity, family hx of BC, hx of benign breast, age at first pregnancy, age at menarche, physical activity, other body size variable

increase risk. A possible dual effect with age was noted for WC and WHR, with higher measurements suggesting a protective effect in younger women (<50 years) and increasing risk in women ≥50 years. In addition, excess weight during adolescence tended to increase risk, although this finding did not achieve statistical significance, likely due to the modest sample size. Weight changes (prior to diagnosis in the cases) did not appear to be associated with breast cancer in this population.

Height

Tall stature has been implicated as a risk factor for breast cancer in White-American females, with somewhat weaker associations generally found in premenopausal women [1]. In a review of seven large prospective cohort studies, the multivariate-adjusted relative risk (RR) of breast cancer per 5 cm increment of height was 1.02 (0.96, 1.10) in premenopausal women and 1.07 (1.03, 1.12) among women of postmenopausal status [1]. It should be noted, however, that some studies have reported stronger associations of increased height with breast cancer among younger women [2, 4], whereas still others have found no association at all with height in pre- or postmenopausal women of European descent [8, 12, 16]. Although investigations of the relationship between height and breast cancer have been scarce among women of African origin, existing studies tend to indicate that height plays a role. Based on the existing literature, the underlying relationship is, however, still unclear. A case–control study of 234 breast cancer cases and 273 controls in Nigeria found significant associations in both pre- and postmenopausal women [17], whereas the Carolina Breast Cancer Study (CBCS), which included 350 African-American cases and 353 African-American controls, reported a positive relationship between height and breast cancer in premenopausal but not postmenopausal women [12]. A third study found no increase in risk of breast cancer associated with tall stature, but a significant decrease in risk among shorter women (<61 inches) compared with those between 64 and 65 inches tall (RR = 0.5 (0.3, 0.7)) [18]. The BNCS analyses indicate that tall stature is positively associated with breast cancer in this population, particularly among women ≥50 years of age. Height, representing intrauterine, early childhood as well as the level of the adolescent growth spurt, likely relates to factors such as nutrition, genetic growth potential, and hormones thus influencing breast cancer occurrence [19–22]. One possible explanation is that taller women may have higher levels of insulin-like growth factors (IGF), which may underlie the link to breast cancer risk [19]. This potential relationship warrants further evaluation, particularly given the higher prevalence of diabetes/hyperinsulinemia in westernized populations of African origin.

BMI

Obesity is more prevalent in African-American than White-American populations, [23] and BMI has been implicated as a factor for influencing breast cancer risk in both pre- and postmenopausal women [1, 3]. The majority of investigations, however, have included primarily Caucasian populations, with a scarcity of studies conducted in populations of African descent [12, 24–26]. Of those that included African women, the findings have not been altogether consistent. In one case–control study including 304 African-American breast cancer cases and 305 African-American controls, BMI was positively associated with breast cancer risk in both pre- and postmenopausal women [25]. In the CBCS, BMI was inversely related to breast cancer risk in premenopausal White-American women but not among premenopausal African-American women [12]. Interestingly, when the CBCS participants were stratified by age (not menopausal status), younger African-American women were found to have an inverse relationship between breast cancer risk and BMI. That study reported no relationship for postmenopausal White-American or African-American women. The prospective Black Women's Health Study reported an inverse association of current BMI among premenopausal women, with no association among those who were postmenopausal [9], whereas a hospital-based case–control study of 234 cases and 273 controls in Nigeria found no association between obesity and breast cancer, regardless of menopausal status. [26] In the BNCS, where more than one-third of both cases and controls had a BMI ≥ 30 kg/m^2, the multivariate analyses indicated that BMI did not seem to impact breast cancer risk in younger or older women.

Waist circumference

Although measures of central adiposity have not been studied as extensively as height, weight, and BMI, the reports that do exist, which have also included predominantly Caucasian participants, indicate that body circumferences may influence breast cancer risk, with the effect possibly being modified by HRT use [6, 27]. In the Women's Health Initiative (WHI) study, WC was associated with breast cancer risk among postmenopausal women, but only in those who never used HRT. The study included only 5–8% of women of African ancestry and, the analyses were not stratified by race/ethnicity [6]. As such, it is unclear whether the influence of WC on breast cancer risk is similar in White-American and African-American females. In the Nurses Health Study (NHS), which also included predominantly White-American women, larger WC increased breast cancer risk in postmenopausal women but no association was found in those who were premenopausal [27]. The multivariate RR for older women in the highest (vs lowest) quintile was 1.34 (1.05, 1.72). The finding was even more pronounced when only those who never used HRT were considered (RR = 1.88 (1.25, 2.85)). Findings from the present investigation suggest the presence of a dual effect for WC on breast cancer risk in African-Barbadian women. Those who were 50 years of age or older and above the highest quintile of WC measurements were found to have a 3-fold risk of breast cancer as compared to older women below the lowest quintile. Although this finding did not reach statistical significance, the risk increased 4-fold and was statistically significant when only older women who never used HRT were considered. Alternatively, younger women (<50 years) with WC above the highest quintile tended to have a reduced risk of breast cancer, as indicated by the markedly low OR = 0.45. Although this finding was not statistically significant, it is likely due to the small sample size in this group. One hypothesis proposed to explain the potentially protective effect among premenopausal women is that obese women of childbearing age may experience amenorrhea or shortened luteal phases in their menstrual cycles, resulting in a decrease in progesterone production. This reduction of progesterone may result in a lesser degree of breast cell mitosis and a subsequent protection against breast cancer [28–30]. Additional research is necessary, however, to confirm or refute this theory.

Waist–hip ratio

WHR has been shown to have no association with breast cancer risk in premenopausal women [27, 31], with less consistent findings in women of postmenopausal status [6, 27, 31]. Although no association was found in postmenopausal women in the WHI study [6], the RR for postmenopausal women in the highest quintile (compared to the lowest quintile) in the NHS was 1.28 (1.02, 1.61) [27]. This finding was corroborated in an African population in Nigeria where the multivariate OR was 2.67 (1.05, 6.80) for postmenopausal women with WHR measurements in the highest tertile compared to those in the lowest [31]. In the BNCS, a dual effect was suggested for women <50 and ≥50 years of age, with younger women experiencing a protective effect from higher WHR values and older women being at increased risk. Tests of interaction between age and WHR in the BNCS further support the noted effect.

Strengths and limitations

The strengths of the BNCS include (but are not limited to) the standardized and comprehensive study protocols, high participation rates among cases and controls, and its nationwide representative sample. The study also represents the first of its kind in the region, thus providing new risk factor data on an understudied population. Although accurate anthropometric measurements were taken at the study visit, one of the limitations of this and other similar studies of body size and cancer is that these measurements could have been affected by the disease itself, a potential problem that the study design was unable to address. A second limitation was the lack of available clinical weight history data for time periods prior to the diagnosis of disease. As such, we had to rely on information based on self-report, which may be influenced by recall bias. It has been documented, however, that self-reported information, especially relating to weight, can be quite accurate [32–36] and can serve as a relatively reliable proxy in investigations of this type. Another limitation of this study is the sizable amount of unavailable weight history data relating to body size variables such as weight at age 15 years, for example. However, despite the reduced sample sizes and the associated loss of power, especially among premenopausal women, the data are indicative of significant or suggestive findings. Although caution must be exercised with respect to the generalizability of the BNCS results beyond this population, the findings warrant further investigation in other populations of African origin.

Conclusions

Data from the BNCS indicate that several body size factors may be important predictors of breast cancer risk in populations of African origin. Tall stature was found to increase breast cancer risk, and a dual effect by age was suggested for WC and WHR in African-Barbadian women, especially among non-HRT users. Higher measurements of WC and WHR yielded a significantly increased breast cancer risk in older women, while suggesting a protective effect in younger women. BMI did not influence risk in this population, where obesity is highly prevalent. These data suggest that a few, but not all body size factors may play a role in breast cancer risk, and that age may affect these relationships. Comparisons of breast cancer rates among women of African origin indicate that those residing in Barbados represent an intermediate population between West African women and those living in the United States [37]. Because both genetic and environmental factors contribute to body size and subsequently breast cancer risk, the BNCS data may be a valuable resource in unraveling breast cancer etiology and in developing strategies for the prevention of this disease among women of African descent.

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