# Original Contribution 

# Case-Control Study of Body Size and Breast Cancer Risk in Nigerian Women 

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#### Abstract

Previous studies have shown that weight is inversely associated with premenopausal breast cancer and positively associated with postmenopausal disease. Height has been shown to be positively correlated with breast cancer risk, but the association was not conclusive for premenopausal women. These previous studies were conducted primarily in Western countries, where height is not limited by nutritional status during childhood. The authors assessed the association between breast cancer and anthropometric measures in the Nigerian Breast Cancer Study (lbadan, Nigeria). Between 1998 and 2009, 1,233 invasive breast cancer cases and 1,101 controls were recruited. The multivariateadjusted odds ratio for the highest quartile group of height relative to the lowest was 2.03 ( $95 \%$ confidence interval (CI): 1.51, 2.72; $P$-trend $<0.001$ ), with an odds ratio of 1.22 ( $95 \% \mathrm{Cl}: 1.14,1.32$ ) for each 5 -cm increase, with no difference by menopausal status. Comparing women with a body mass index in the lowest quartile group, the adjusted odds ratio for women in the highest quartile category was 0.72 ( $95 \% \mathrm{Cl}: 0.54,0.94 ; P$-trend $=0.009$ ) for premenopausal and postmenopausal women. Influence of height on breast cancer risk was quite strong in this cohort of indigenous Africans, which suggests that energy intake during childhood may be important in breast cancer development.


Africa; body height; body mass index; breast neoplasms

Abbreviation: BMI, body mass index.

Breast cancer ranks second in global cancer incidence and is the most common cancer diagnosis among Nigerian women (1-4). While breast cancer incidence has been shown to have stabilized or to be decreasing in some Western countries, the breast cancer burden has steadily increased in many developing countries with traditionally low incidence rates $(5,6)$. Among factors proposed to contribute to the rising incidence in these societies are secular changes in lifestyle and reproductive factors.

The influence of anthropometric measures on breast cancer risk has been the subject of many studies (7-13). The relation between body weight and breast cancer risk is modified by menopausal status, with higher weight or body mass index (BMI) associated with increased risk for postmenopausal women and reduced risk for premenopausal women. Height is linked to increased breast cancer risk for postmenopausal women, and the association is less clear for premenopausal women. However, these findings were derived from studies conducted mainly in Western
countries, where the prevalence of obesity is relatively high and attained height is not limited by nutritional status in childhood. Therefore, the influence of body size on breast cancer risk in developing countries remains unclear.

Nigerian women have a low prevalence of obesity (14), and childhood growth in developing countries can be limited by energy deprivation (15). A demographic and health survey conducted in 1990 estimated that the prevalence of stunting was $43 \%$ in Nigerian children (15). Therefore, breast cancer cases and controls from Nigeria provide a unique opportunity to evaluate the association of weight and height with breast cancer risk. Using data from our pilot study (16), we previously reported a positive association of height with breast cancer risk but no significant association between weight or BMI and breast cancer risk for urbanized Nigerian women. However, the sample size was much smaller in this pilot study. Here, we present findings from an analysis of more than 1,000 cases and 1,000 controls from the ongoing Nigerian Breast Cancer Study.

Table 1. Selected Characteristics of Cases With Invasive Breast Cancer and Community Controls, Nigeria, 1998-2009

| Characteristic | Cases ( $n=1,233$ ) |  |  | Controls ( $n=1,101$ ) |  |  | $\underset{\text { Value }}{P}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Mean (SD) | No. | \% | Mean (SD) | No. | \% |  |
| Age, years | 47.0 (11.5) |  |  | 40.8 (12.8) |  |  | <0.001 |
| Ethnicity ${ }^{\text {a }}$ |  |  |  |  |  |  | <0.001 |
| Yoruba |  | 903 | 73.2 |  | 1,045 | 94.9 |  |
| lbo |  | 157 | 12.7 |  | 25 | 2.3 |  |
| Hausa |  | 19 | 1.5 |  | 1 | 0.1 |  |
| Others |  | 154 | 12.5 |  | 30 | 2.7 |  |
| Education |  |  |  |  |  |  | 0.001 |
| No formal |  | 271 | 22.0 |  | 170 | 15.4 |  |
| Elementary |  | 293 | 23.8 |  | 172 | 17.5 |  |
| Secondary |  | 221 | 17.9 |  | 264 | 21.5 |  |
| Vocational |  | 170 | 13.8 |  | 137 | 12.8 |  |
| Some college or above |  | 277 | 22.5 |  | 357 | 32.7 |  |
| Marital status |  |  |  |  |  |  | 0.15 |
| Married |  | 1,056 | 85.7 |  | 921 | 91.1 |  |
| Single |  | 29 | 2.4 |  | 112 | 2.7 |  |
| Divorced/separated |  | 25 | 2.0 |  | 10 | 1.0 |  |
| Widowed |  | 122 | 9.9 |  | 59 | 5.3 |  |
| Family history of breast cancer |  | 99 | 8.0 |  | 51 | 4.3 | <0.001 |
| Benign breast disease |  | 107 | 8.7 |  | 45 | 4.6 | <0.001 |
| Age at menarche, years | 15.2 (2.1) |  |  | 15.3 (2.2) |  |  | 0.018 |
| Menopausal status |  |  |  |  |  |  | 0.09 |
| Premenopausal |  | 707 | 57.4 |  | 820 | 73.6 |  |
| Postmenopausal, natural |  | 498 | 40.4 |  | 266 | 25.1 |  |
| Postmenopausal, artificial |  | 27 | 2.2 |  | 13 | 1.3 |  |
| Age at natural menopause, years | 48.5 (5.4) |  |  | 48.8 (4.9) |  |  | 0.064 |
| No. of livebirths | 4.1 (2.4) |  |  | 3.9 (2.1) |  |  | 0.22 |
| Age at first livebirth, years ${ }^{b}$ | 23.0 (4.7) |  |  | 23.8 (4.2) |  |  | 0.001 |
| Months of lactation ${ }^{\text {b }}$ | 65.4 (42.9) |  |  | 58.8 (35.8) |  |  | 0.96 |
| Hormone contraceptive use |  | 305 | 24.8 |  | 232 | 24.6 | 0.25 |
| Alcohol drinking |  | 137 | 11.4 |  | 65 | 7.2 | 0.001 |

Abbreviation: SD, standard deviation.
${ }^{\text {a }}$ Proportions or means for the controls are adjusted values based on the age distribution of cases; $P$ values were also age adjusted in logistic regressions.
${ }^{\mathrm{b}}$ Among parous women.

## MATERIALS AND METHODS

## Study population

The study protocol was approved by the institutional review boards of the University of Chicago (Illinois) and the University of Ibadan (Nigeria). The Nigerian Breast Cancer Study is a case-control study of breast cancer conducted in

Ibadan, Nigeria. The study setting and design have been described previously (16, 17). Briefly, all consecutive female breast cancer patients aged 18 years or older attending the surgical oncology and radiotherapy clinics of the University College Hospital, Ibadan, Nigeria, from 1998 to 2009 were approached. The majority of eligible patients provided written consent to participate in the study, with

Table 2. Association Between Height and Risk of Breast Cancer in Nigerian Women, 19982009

| Height, cma | Cases | Controls | $\begin{gathered} \text { Age-adjusted } \\ \text { OR } \end{gathered}$ | 95\% CI | Adjusted OR ${ }^{\text {b }}$ | 95\% CI |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total |  |  |  |  |  |  |
| <155 [151] | 221 | 262 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 155-159 [157] | 323 | 352 | 1.14 | 0.89, 1.46 | 1.22 | 0.94, 1.60 |
| 160-164 [162] | 347 | 287 | 1.60 | 1.24, 2.06 | 1.75 | 1.33, 2.30 |
| $\geq 165$ [168] | 299 | 197 | 1.98 | 1.51, 2.59 | 2.03 | 1.51, 2.72 |
| $P$ for trend |  |  | <0.001 |  | <0.001 |  |
| Mean (SD) | 160.2 (6.8) | 158.8 (6.4) |  |  |  |  |
| Per 5 cm |  |  | 1.22 | 1.14, 1.30 | 1.22 | 1.14, 1.32 |
| Premenopausal |  |  |  |  |  |  |
| <155 [152] | 103 | 175 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 155-159 [157] | 170 | 260 | 1.10 | 0.80, 1.52 | 1.21 | 0.85, 1.73 |
| 160-164 [162] | 207 | 230 | 1.55 | 1.12, 2.13 | 1.60 | 1.12, 2.28 |
| $\geq 165$ [168] | 204 | 155 | 2.16 | 1.55, 3.02 | 2.11 | 1.46, 3.05 |
| $P$ for trend |  |  | <0.001 |  | <0.001 |  |
| Mean (SD) | 161.2 (6.6) | 159.2 (6.3) |  |  |  |  |
| Per 5 cm |  |  | 1.25 | 1.15, 1.36 | 1.23 | 1.13, 1.35 |
| Postmenopausal |  |  |  |  |  |  |
| <155 [151] | 118 | 87 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 155-159 [157] | 153 | 92 | 1.20 | 0.82, 1.75 | 1.23 | 0.82, 1.84 |
| 160-164 [161] | 140 | 57 | 1.79 | 1.18, 2.73 | 2.09 | 1.34, 3.25 |
| $\geq 165$ [167] | 95 | 42 | 1.60 | 1.00, 2.55 | 1.75 | 1.06, 2.88 |
| $P$ for trend |  |  | 0.009 |  | 0.002 |  |
| Mean (SD) | 158.9 (6.9) | 157.4 (6.5) |  |  |  |  |
| Per 5 cm |  |  | 1.17 | 1.05, 1.31 | 1.20 | 1.07, 1.36 |
| $P$ for interaction ${ }^{\text {c }}$ |  |  | 0.39 |  | 0.88 |  |

Abbreviations: CI , confidence interval; OR, odds ratio; ref., referent; SD, standard deviation.
${ }^{\text {a }}$ Midpoints of categories are given in brackets.
${ }^{\mathrm{b}}$ Adjusted for age at diagnosis or interview, ethnicity, education, age at menarche, number of livebirths, age at first livebirth, duration of breastfeeding, menopausal status, age at menopause, family history of breast cancer, benign breast disease, hormonal contraceptive use, and alcohol drinking.
${ }^{\text {c }}$ Interaction between height and menopausal status.
a refusal rate of only $4 \%$. University College Hospital serves a population of 3 million people in Ibadan and is a referral center for other hospitals in the region. Based on data from the Ibadan Cancer Registry, about $60 \%$ of all breast cancer cases diagnosed in Ibadan are seen at University College Hospital, and the age distribution was similar between patients enrolled and those not enrolled.

Eligible controls were females aged 18 years or older, who were free of cancer, provided written consent to participate in the study, and were from a community in the city of Ibadan. Residents of this community were considered to have demographic characteristics similar to those of the patients who present to the University College Hospital. A stable, socioeconomically diverse community adjoining the hospital was randomly selected by ballot from a list of all communities in the area. Names were randomly selected from the census-derived community register. Because of the engagement of community leaders in the study, nearly
$98 \%$ of individuals in the community invited for the study chose to participate. Recruitment of the cases and the controls was carried out by trained research nurses at the outpatient clinics of University College Hospital and in a designated community center, respectively. Cases were recruited at or soon after presentation following clinical and histologic confirmation of breast cancer.

## Data collection and measures

Information on demographics, family history of breast cancer and history of benign breast disease, lifestyle factors, menstrual and reproductive history, and hormonal contraceptive use was elicited from participants by means of structured questionnaires administered by the research nurses. Research nurses also measured weight, height, and waist and hip circumferences. We examined height, weight, and BMI in relation to breast cancer risk. BMI was


Figure 1. Multivariate-adjusted odds ratios and $95 \%$ confidence intervals for breast cancer according to quartiles of body height in Nigerian women, 1998-2009. A) All women, B) premenopausal women, C) postmenopausal women.
calculated as weight in kilograms divided by height in meters squared. Based on equally spaced boundaries, height ( $<155,155-159,160-164, \geq 165 \mathrm{~cm}$ ) and weight ( $<55$, $55-64,65-74, \geq 75 \mathrm{~kg}$ ) were grouped into 4 categories, which are also close to the quartiles of the sample. BMI was classified by using cutoff points of $<21,21-23.9,24-$ 27.9 , and $\geq 28 \mathrm{~kg} / \mathrm{m}^{2}$ based on quartiles of the study sample.

The following potential confounders were categorized and were adjusted for: age at diagnosis or interview (5-year-interval categories), ethnicity (Yoruba, others), education (none, elementary, secondary, vocational, and some college or above), age at menarche, number of livebirths ( $0,1-3,4-6, \geq 7$ ), age at first livebirth, duration of breastfeeding ( $0-24,25-48,49-72,>72$ months), first-degree family history of breast cancer (yes, no), benign breast disease (yes, no), hormonal contraceptive use (ever, never), alcohol drinking (yes, no), and menopausal status (premenopausal, naturally postmenopausal, artificially postmenopausal). Alcohol intake was defined as consumption of alcoholic beverages at least once a week for 6 months or longer. Natural menopause was defined as cessation of menstrual periods for 1 year or more, and artificial menopause was considered menopause after surgery or other medical treatment. The use of postmenopausal hormone replacement therapy by Nigerian women is rare (only one woman in our sample), so we did not adjust for it in the analysis.

## Statistical analysis

Demographic or potential confounders were compared between cases and controls by using $t$ tests or Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical data. Pearson correlation coefficients were calculated to describe the interrelation between anthropometric measures. Logistic regression models were used to examine the relation between anthropometric measures and
breast cancer. Odds ratios and $95 \%$ confidence intervals were computed as measures of association from the logistic models. Multiple logistic regressions were fitted to adjust for age and the other potential confounders listed above. The anthropometric variables were entered in the models as continuous or categorical. Analyses were conducted for all women and separately for premenopausal and naturally postmenopausal women.

About $6 \%$ of participants had a missing value for age at menarche, and $2 \%$ of them had missing values for height and weight. Data were occasionally missing for other variables as well. To use all available information and avoid bias due to listwise deletion in the multivariate analysis, we imputed missing values 20 times via the method of multiple imputation by chained equations (18). Standard errors of regression coefficients were determined by using Rubin's general formula for combining estimates in multiple imputation (19). Multiple imputation assumes that data are missing at random (19). Missing menarcheal age was due to poor memory, and older women tended to forget their menarcheal age. After age was included in the multiple imputation models, it is reasonable to think that the probability of missing menarcheal age was unrelated to the missed value itself. Multiple imputation was conducted by using the ice module in Stata software developed by P. Royston (20). All $P$ values were 2-sided. Statistical analyses were conducted with Stata 10.0 software (StataCorp, College Station, Texas).

## RESULTS

The study included 1,233 women diagnosed with invasive breast cancer and 1,101 community controls. Table 1 shows selected characteristics of study participants. Women with breast cancer were older than the controls. About $60 \%$ of cases were younger than age 50 years, and $16 \%$ were aged

Table 3. Association Between Weight and Risk of Breast Cancer in Nigerian Women, 19982009

| Weight, $\mathrm{kg}^{\text {a }}$ | Cases | Controls | $\begin{gathered} \hline \text { Age-adjusted } \\ \text { OR } \end{gathered}$ | 95\% CI | Adjusted $\mathbf{O R}^{\mathrm{b}}$ | 95\% CI |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total |  |  |  |  |  |  |
| <55 [50] | 286 | 321 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 55-64 [60] | 341 | 330 | 0.97 | 0.77, 1.23 | 0.86 | 0.67, 1.12 |
| 65-74 [69] | 262 | 228 | 1.01 | 0.79, 1.30 | 0.82 | 0.62, 1.09 |
| $\geq 75$ [83] | 299 | 218 | 1.08 | 0.84, 1.39 | 0.82 | 0.62, 1.10 |
| $P$ for trend |  |  | 0.45 |  | 0.20 |  |
| Mean (SD) | 65.8 (14.8) | 63.2 (13.5) |  |  |  |  |
| Per 10 kg |  |  | 1.04 | 0.98,1.11 | 0.98 | 0.91, 1.05 |
| Premenopausal |  |  |  |  |  |  |
| <55 [50] | 159 | 253 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 55-64 [60] | 196 | 257 | 0.96 | 0.72, 1.28 | 0.81 | 0.59, 1.11 |
| 65-74 [69] | 156 | 158 | 1.15 | 0.84, 1.58 | 0.89 | 0.63, 1.26 |
| $\geq 75$ [83] | 172 | 151 | 1.18 | 0.86, 1.62 | 0.78 | 0.55, 1.12 |
| $P$ for trend |  |  | 0.17 |  | 0.27 |  |
| Mean (SD) | 65.9 (14.3) | 62.6 (13.2) |  |  |  |  |
| Per 10 kg |  |  | 1.06 | 0.98,1.15 | 0.95 | 0.87, 1.04 |
| Postmenopausal |  |  |  |  |  |  |
| <55 [50] | 127 | 68 | 1.0 (ref.) | 1.0 (ref.) |  |  |
| 55-64 [60] | 145 | 73 | 0.99 | 0.66, 1.50 | 0.98 | 0.63, 1.52 |
| 65-74 [69] | 106 | 70 | 0.81 | 0.53, 1.23 | 0.72 | 0.46, 1.14 |
| $\geq 75$ [84] | 127 | 67 | 0.95 | 0.62, 1.45 | 0.90 | 0.57, 1.44 |
| $P$ for trend |  |  | 0.66 |  | 0.48 |  |
| Mean (SD) | 65.7 (15.4) | 65.0 (14.1) |  |  |  |  |
| Per 10 kg |  |  | 1.02 | 0.92, 1.13 | 1.02 | 0.91, 1.13 |
| $P$ for interaction ${ }^{\text {c }}$ |  |  | 0.24 |  | 0.89 |  |

Abbreviations: CI , confidence interval; OR, odds ratio; ref., referent; SD, standard deviation.
${ }^{\text {a }}$ Midpoints of categories are given in brackets.
${ }^{\mathrm{b}}$ Adjusted for age at diagnosis or interview, ethnicity, education, age at menarche, number of livebirths, age at first livebirth, duration of breastfeeding, menopausal status, age at menopause, family history of breast cancer, benign breast disease, hormonal contraceptive use, alcohol drinking, and height.
${ }^{\text {c }}$ Interaction between weight and menopausal status.

60 years or older. Because age was a potential confounder, and results from univariate analysis may be misleading, we calculated expected proportions or means in the control group according to the age distribution of cases, along with age-adjusted $P$ values (Table 1). The majority of study participants were Yoruba (other ethnicities include Hausa and Ibo), which reflects the ethnic breakdown of the population in southwestern Nigeria. There were more Yoruba controls than Yoruba cases. Cases and controls were also different regarding education. Compared with controls, cases were more likely to have a family history of breast cancer, to have a history of benign breast disease, and to have consumed alcohol. Cases and controls were similar in terms of marital status and use of hormonal contraceptives. The distributions of some reproductive factors, including age at menarche and age at first livebirth, were different between cases and controls; detailed analysis results of reproductive factors can be found in our previous paper (17). All these variables were
considered potential confounders and were adjusted for in subsequent analyses.

Height was weakly correlated with body weight ( $r=$ 0.22 ) and BMI ( $r=-0.16$ ). BMI was strongly correlated with body weight $(r=0.92)$. As depicted in Table 2, cases were on average $1.4-\mathrm{cm}$ taller ( 160.2 cm (standard deviation, 6.8), range: 130-185) than controls ( 158.8 cm (standard deviation, 6.4), range: 138-186). For all women, a significant positive linear relation existed between height and breast cancer risk. The multivariate-adjusted odds ratio comparing those in the highest category ( $\geq 165 \mathrm{~cm}$ ) with those in the lowest category $(<155 \mathrm{~cm})$ of height was 2.03 ( $95 \%$ confidence interval: $1.51,2.72 ; P$-trend $<0.001$ ). For every $5-\mathrm{cm}$ increase in height, the risk of breast cancer increased by $22 \%$ (odds ratio $=1.22,95 \%$ confidence interval: $1.14,1.32$ ). The positive and linear association existed for both premenopausal and postmenopausal women (Figure 1).

Table 4. Association Between Body Mass Index and Risk of Breast Cancer in Nigerian Women, 1998-2009

| Body mass index, | Cases | Controls | $\begin{gathered} \text { Age-adjusted } \\ \text { OR } \end{gathered}$ | 95\% CI | Adjusted OR ${ }^{\text {b }}$ | 95\% CI |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Total |  |  |  |  |  |  |
| <21 [19.4] | 253 | 268 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 21-23.9 [22.5] | 287 | 256 | 0.99 | 0.76, 1.28 | 0.93 | 0.71, 1.23 |
| 24-27.9 [26.0] | 309 | 282 | 0.86 | 0.67, 1.11 | 0.79 | 0.60, 1.04 |
| $\geq 28$ [31.4] | 338 | 291 | 0.81 | 0.63, 1.04 | 0.72 | 0.54, 0.94 |
| $P$ for trend |  |  | 0.052 |  | 0.009 |  |
| Mean (SD) | 25.7 (5.6) | 25.1 (5.4) |  |  |  |  |
| Per $5 \mathrm{~kg} / \mathrm{m}^{2}$ |  |  | 0.96 | 0.88, 1.04 | 0.93 | 0.85, 1.01 |
| Premenopausal |  |  |  |  |  |  |
| <21 [19.5] | 153 | 219 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 21-23.9 [22.4] | 172 | 202 | 1.00 | 0.73, 1.36 | 0.89 | 0.64, 1.24 |
| 24-27.9 [26.0] | 170 | 206 | 0.86 | 0.63, 1.16 | 0.74 | 0.53, 1.04 |
| $\geq 28$ [31.2] | 187 | 192 | 0.88 | 0.64, 1.20 | 0.70 | 0.50, 0.98 |
| $P$ for trend |  |  | 0.31 |  | 0.027 |  |
| Mean (SD) | 25.4 (5.4) | 24.7 (5.2) |  |  |  |  |
| Per $5 \mathrm{~kg} / \mathrm{m}^{2}$ |  |  | 0.96 | 0.87, 1.06 | 0.89 | 0.79, 0.99 |
| Postmenopausal |  |  |  |  |  |  |
| <21 [19.3] | 100 | 49 | 1.0 (ref.) |  | 1.0 (ref.) |  |
| 21-23.9 [22.6] | 115 | 54 | 0.95 | 0.59, 1.53 | 1.04 | 0.63, 1.71 |
| 24-27.9 [26.0] | 139 | 76 | 0.85 | 0.54, 1.32 | 0.88 | 0.55, 1.41 |
| $\geq 28$ [31.6] | 151 | 99 | 0.71 | 0.46, 1.09 | 0.76 | 0.48, 1.21 |
| $P$ for trend |  |  | 0.07 |  | 0.15 |  |
| Mean (SD) | 26.1 (5.9) | 26.3 (5.7) |  |  |  |  |
| Per $5 \mathrm{~kg} / \mathrm{m}^{2}$ |  |  | 0.96 | 0.84, 1.08 | 0.98 | 0.86, 1.12 |
| $P$ for interaction ${ }^{\text {c }}$ |  |  | 0.37 |  | 0.85 |  |

Abbreviations: CI , confidence interval; OR , odds ratio; ref., referent; SD, standard deviation.
${ }^{\text {a }}$ Midpoints of categories are given in brackets.
${ }^{\mathrm{b}}$ Adjusted for age at diagnosis or interview, ethnicity, education, age at menarche, number of livebirths, age at first livebirth, duration of breastfeeding, menopausal status, age at menopause, family history of breast cancer, benign breast disease, hormonal contraceptive use, and alcohol drinking.
${ }^{c}$ Interaction between BMI and menopausal status.

Mean weight was 65.8 kg (standard deviation, 14.8; range: $34-160$ ) in breast cancer patients and 63.2 kg (standard deviation, 13.5; range: 38-117) in controls, but the difference was confounded by age. In multivariate analysis adjusting for potential confounders, no statistically significant association was found between weight and breast cancer risk (Table 3). However, there was a statistically significant association between BMI and breast cancer risk, as depicted in Table 4. Compared with women with a BMI of $<21 \mathrm{~kg} / \mathrm{m}^{2}$, women with a BMI of $\geq 28 \mathrm{~kg} / \mathrm{m}^{2}$ had $28 \%$ reduced odds of having breast cancer (odds ratio $=0.72$, $95 \%$ confidence interval: 0.54, $0.94 ; P$-trend $=0.009$ ). Modeling BMI as a continuous variable showed that the odds of having breast cancer decreased by $8 \%$ for every 5 -unit increase in BMI (odds ratio $=0.93,95 \%$ confidence interval: $0.85,1.01$ ). This inverse relation appeared for both premenopausal and postmenopausal women, although it did not reach statistical significance for postmenopausal women
(Figure 2). The interaction between menopausal status and BMI was not significant ( $P=0.85$ ).

## DISCUSSION

In this study of anthropometric measures in an indigenous African population, we demonstrated that height was a significant risk factor for female breast cancer in both premenopausal and postmenopausal women. This study did not find a significant relation between body weight and breast cancer risk but found an inverse relation between BMI and breast cancer risk.

The strength of association between height and breast cancer risk for Nigerians was much stronger than that observed in Western countries. In a pooled analysis of 7 cohort studies, the relative risk for each $5-\mathrm{cm}$ increase in height was 1.02 for premenopausal women and 1.07 for postmenopausal women, and the relative risk for women 175 cm


Figure 2. Multivariate-adjusted odds ratios and $95 \%$ confidence intervals for breast cancer according to quartiles of body mass index in Nigerian women, 1998-2009. A) All women, B) premenopausal women, C) postmenopausal women.
or taller compared with those shorter than 160 cm was 1.42 for premenopausal women and 1.28 for postmenopausal women (8). Similar findings were observed in a large case-control study conducted in the United States (21). In contrast, we found that the relative risk per $5-\mathrm{cm}$ increase was 1.22, and the relative risk for Nigerian women 165 cm or taller compared with those shorter than 155 cm was 2.03 (similar for premenopausal and postmenopausal women). Attained height is determined by genetic makeup and environmental factors, including energy intake during childhood and adolescence. In societies with an insufficient food supply, caloric intake plays a more important role in determining height than in societies with an abundant food supply. Shorter height in our study population may be due to energy deprivation in childhood and adolescence (15). In a study conducted in China, the effect of height was stronger for postmenopausal women than for premenopausal women, and many postmenopausal women grew up during periods when the supply of food was limited (22). Similarly, a cohort study in Norway documented a stronger effect between height and breast cancer in women who experienced their peripubertal growth during World War II (23). Furthermore, a cohort study showed that early growth spurts during childhood and adolescence independently affected breast cancer risk (24). Taken together, these studies suggest that energy intake early in life plays an important role in breast carcinogenesis. The underlying mechanism could be that childhood energy balance is associated with mammary gland mass and increased insulin-like growth factors ( 25,26 ).

The inverse association between BMI and breast cancer in premenopausal Nigerian women was consistent with many previous studies, but not all. We found that the odds ratio for a $5-\mathrm{kg} / \mathrm{m}^{2}$ increase in BMI was 0.89 for Nigerians. A pooled analysis of 7 cohort studies showed that the relative risk was 0.89 for each $4-\mathrm{kg} / \mathrm{m}^{2}$ increase in BMI (8). A large casecontrol study conducted in the United States showed an odds
ratio of 0.98 for a $1-\mathrm{kg} / \mathrm{m}^{2}$ increase in BMI (21). A cohort study in African Americans also showed that BMI was associated with reduced risk of breast cancer (27). In contrast, one study conducted in the 1960 s showed that BMI was positively correlated with premenopausal breast cancer risk in low-risk societies including Japan and Taiwan (10). Obese women experience menstrual irregularities characterized by anovulatory cycles, with consequent low circulating hormone levels (28). Moreover, obesity is associated with hyperinsulinemia, which interferes with ovarian follicular development and function (25).

BMI was inversely, although not statistically significantly, associated with risk of postmenopausal breast cancer in the present study. This finding is inconsistent with previous studies conducted in white and Asian populations, in which a positive association was observed (8, 10, 22, 29). However, several studies of African Americans also found inconsistent results, with high BMI being associated with an increased risk of postmenopausal breast cancer in 2 studies $(30,31)$, reduced risk in 2 studies $(32,33)$, and no association in 3 studies (27, 34, 35). Admittedly, the association between BMI and risk of breast cancer in postmenopausal women was weak even for studies that showed a positive association; for example, one pooled analysis found that the relative risk was only 1.07 for each $4-\mathrm{kg} / \mathrm{m}^{2}$ increase in BMI (8). Most of the postmenopausal women in this study were in their fifties, so it takes time for the benefit of premenopausal overweight to disappear after menopause. Alternatively, overweight or obesity may not be an important risk factor for postmenopausal breast cancer in women of African ancestry, as suggested by the inconsistent findings from studies of African Americans. However, evidence is mounting that this association is present for only hormone-receptor-positive tumors $(36,37)$. It is documented that black women living in the United States, the United Kingdom, and Africa are more likely than their white
counterparts to have estrogen-receptor-negative breast cancers (38-40). Therefore, the association of body weight with postmenopausal breast cancer deserves further investigation by breast cancer subtypes and across different populations.

To our knowledge, this is the largest case-control study of anthropometric measures and breast cancer from an indigenous African population, which provided adequate power to explore these associations. Another strength of our study is that body sizes were actually measured by the research nurses rather than self-reported, thereby enhancing validity. Nonetheless, several possible limitations should be considered when interpreting our study findings. Cases were significantly older than controls because controls were randomly selected from the community and were not matched on age. We found age to be the single most important confounder in the analysis, but it was sufficiently adjusted for in the multivariate logistic models. We did not record weight in early life such as at age 18 years, so this study was not designed to examine the effect of weight change. Because many women in Nigeria do not know their weight, we could not collect reliable data on weight at age 18 years. We did not collect data on physical activities and have only limited data on hormone receptor status, so these are important areas of future research in this population. Because the majority of subjects are premenopausal women, the study has limited power to assess the relation of weight and postmenopausal breast cancer risk.

The present study provided a unique opportunity to elucidate the impact of anthropometric factors on breast cancer risk in a population in which breast cancer incidence is low and food intake during childhood may have limited growth. We found that attained height was a significant risk factor for breast cancer regardless of menopausal status. The strong influence of height suggests that energy intake in earlier life may play an important role in breast carcinogenesis. We also found an inverse association between BMI and breast cancer risk in premenopausal women and postmenopausal women, but the association for postmenopausal women was not statistically significant. Given that the etiology of breast cancer in African women is only now being revealed, the overrepresentation of young-onset, estrogen-receptor-negative cases in the study population makes this study rather unique. The inverse effect of high weight on breast cancer risk for postmenopausal women underscores the need for other independent studies of African women to determine whether lifestyle interventions such as weight control could be an appropriate strategy to prevent breast cancer in Africa.

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