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ORIGINAL PAPER

Obesity is an initiator of colon adenomas but not a promoter of colorectal cancer in the Black Women's Health Study

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Abstract

Purpose Evidence for the association of anthropometrics with colorectal neoplasms is limited for African Americans.

Methods We examined anthropometric measures with both colorectal adenoma and colorectal cancer (CRC) risk in the ongoing Black Women's Health Study. In a nested case–control analysis, 954 cases of colorectal adenoma were compared with 3,816 polyp-free controls, matched on age and follow-up time. For the CRC analyses, 413 incident CRC cases were identified over a 16-year follow-up (802,783 person-years). Adenoma cases and CRC were verified by medical record review. We used multivariable conditional logistic regression analyses (for adenoma) and Cox proportional hazards analyses (for CRC) that included anthropometric exposures and selected confounders.

Results Overall body mass index (BMI) and other anthropometric factors were not associated with colorectal adenoma or cancer risk in Black women. However, increased risk of adenoma (but not CRC) was observed among especially related to adenomas in the proximal colon. Among women ≥ 50 years of age, risk of proximal adenoma increased 14% (95% CI 1.00, 1.31), 35% (95% CI 1.12, 1.63), and 25% (0.93, 1.68) with each standard deviation increase in BMI, waist circumference, and waist-to-hip ratio, respectively. None of the anthropometric factors were associated with young onset CRC or adenoma risk.

Conclusion Our results suggest that obesity might be an initiator for colon adenomas but not a promoter for colorectal cancer among Black women.

Keywords African american women · Colorectal adenoma · Colorectal cancer · BMI · Obesity

Introduction

Numerous studies have evaluated the association of obesity, primarily body mass index (BMI), with colorectal cancer (CRC), and adenomas [1–4]. Recent studies, including two meta-analyses, suggest that BMI is more strongly associated with CRC and adenomas in men than women [1, 4]. However, it is possible that BMI might not be the most relevant anthropometric measure of obesity-associated colorectal neoplasia risk. Measures of abdominal adiposity, such as waist circumference (WC) and waist-to-hip ratio (WHR), might be more strongly associated with colorectal neoplasia risk than body mass index (BMI) among women.

Abdominal adiposity, through its effects on pro-inflammatory, oxidative stress, and metabolic pathways, has been hypothesized to be a better biological measure of obesity-associated CRC than BMI [5]. Additionally, the positive association of abdominal obesity with estradiol, a significant modulator of the estrogen pathway hypothesized to be involved in colorectal carcinogenesis, provides biological support for waist circumference and WHR as more relevant measures of obesity among women [6].

Anthropometric measures other than BMI and abdominal adiposity have not been well studied as risk factors for CRCs and adenomas. Some studies have suggested adult weight gain as a risk factor for colorectal neoplasms [7]. In addition, given the strong correlation between BMI and WC, it

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has been suggested that the estimation of independent effects of these 2 anthropometric measures as epidemiologic risk factors is difficult even in statistical models that include both factors [8]. A new measure, a body shape index (ABSI), was recently defined as WC/(BMI$^{2/3}$ Height$^{1/2}$) [9]. ABSI was derived as a measure of abdominal adiposity that has little correlation with either weight or BMI.

Relatively few studies have investigated multiple anthropometric measures as risk factors for colorectal adenoma and cancer among women and none have been adequately powered for these analyses among African American women. In a previous analysis from the Black Women's Health Study (BWHS), we found associations of both body mass index (BMI) and waist-to-hip ratio (WHR) with colorectal polyps, but the association with polyp location (proximal versus distal) was not assessed [10]. In the present study, we investigated association of BMI, WC, WHR, weight gain in adulthood, and ABSI with risk of colorectal adenoma and cancer among African American women in the BWHS.

Methods

Study population

The BWHS is a prospective cohort study of African American women from across the United States. In 1995, 59,000 women aged 21 to 69 years enrolled by responding to health questionnaires mailed to subscribers of Essence magazine, members of several African American professional associations, and friends of early respondents [11]. Approximately equal proportions were from the Northeast, South, Midwest, and West [12]. Respondents completed 14-page questionnaires on demographics, health status, and medical and lifestyle variables. The baseline questionnaire obtained information on adult height, current weight, demographic characteristics, reproductive history, medical history, use of medications, use of cigarettes and alcohol, and usual diet. Since 1995, follow-up questionnaires have been sent every two years to update information on reproductive history and other exposures and identify new occurrences of cancer and other serious illnesses. Follow-up of the baseline cohort has been successful with a follow-up rate of eighty-seven percent of all potential person-years through 2013. Approval for the study was obtained from Boston University Institutional Review Board.

Study design

We used a nested case–control design to investigate the association of anthropometric factors with adenoma and a prospective cohort design to investigate the association of anthropometric factors with CRC risk.

Adenoma case and control ascertainment

Participants were asked about a list of diseases and date of first diagnosis on baseline and follow-up questionnaires. In 1999, "colon or rectal polyps" was added to the list of illnesses for which participants were asked to indicate whether they had received a first diagnosis in the previous two years. Women who reported a colon or rectal polyp were asked for permission to obtain medical records relevant to the colonoscopy. Characteristics of all women who reported a polyp were similar to those of women for whom medical records were obtained and confirmed an adenoma. Mean BMI in 1995 and mean waist-to-hip ratio in 1995 are 28.9 kg/m^2 and 0.79 among all women who reported a polyp and 28.5 kg/m^2 and 0.79 among women with a confirmed adenoma.

Cases in the present analyses were colorectal adenomas confirmed by pathology reports and first identified by self-report of colorectal "polyp" on any of the 1999 through 2011 follow-up questionnaires. There were 954 confirmed adenomas from among the 23,804 women who reported a colonoscopy or sigmoidoscopy during the follow-up period from 1997 to 2011 and had not had a colorectal polyp or any cancer at the start of follow-up in 1997.

A risk set sampling approach was used to select controls from among participants who reported undergoing a colonoscopy or sigmoidoscopy but had not reported a colorectal polyp during or prior (<10 years) to the follow-up period in which the index case reported an incident adenoma diagnosis. Four controls were randomly selected from the list of eligible controls, matched to cases on age and follow-up period at the time of adenoma diagnosis. Relevant exposure data for the controls were abstracted from the questionnaires prior to the "index period" (year for which the index case reported a polyp). Women with cancer (including colorectal cancer), polyps other than adenomas, and women for whom a medical record for polyp review could not be obtained, were excluded from the analysis.

CRC case ascertainment

Colon and rectal cancer cases (ICD-10 colon cancer: C18.0–C18.9 and C26.0; ICD-10 rectal cancer: C19.9 and C20.9) were identified for follow-up from 1995 to 2011 through self-report on the follow-up questionnaires, through linkage with cancer registries in 24 states in which 95% of participants live, and through death records. Pathology data were obtained from hospitals or registries for confirmation. To date, of 397 self-reported cases occurring in the BWHS during follow-up for which pathology data were obtained, 394 (99%) were confirmed as colorectal cancer. Given the accuracy of self-report, all self-reported cases were included in the present analyses unless found to be incorrectly reported based on pathology data.

Assessment of anthropometric factors

In 1995, we collected information on self-reported height (in feet and inches), current weight (in pounds), and weight at age 18 (in pounds). We also asked each participant to measure her waist circumference at the level of the umbilicus (in inches) and hip circumference at its widest location (in inches). Current weight was updated every 2 years by follow-up questionnaire and waist/hip circumferences were updated in 2005. Height (1995) and current weight were used to calculate body mass index (BMI) (kg/m^2); waist circumference was divided by hip circumference to calculate WHR; and adult weight change was calculated by subtracting weight at age 18 from participant-reported current weight. ABSI was calculated using the following formula: WC/(BMI$^{2/3}$ height$^{1/2}$), where WC and height are in m, and BMI is in kg/m^2. Self-reported weight (Spearman correlation = 0.97) and height (Spearman correlation = 0.93) were highly correlated with technician measurements in a BWHS validation study [13, 14].

Assessment of covariates

Covariates for analysis were selected a priori from the literature. Data on age, education, cigarette smoking, regular (at least 3 days a week) aspirin use, alcohol intake, menopausal status, and postmenopausal hormone therapy were collected on the baseline questionnaire (1995) and updated based on data reported on the follow-up questionnaires. In the 1997 and subsequent questionnaires, participants provided information on the number of hours spent each week on vigorous exercise such as basketball, swimming, running and aerobics. Information on education was obtained in 1995 and information on family history of colorectal cancer in a first-degree relative was obtained in 1999. Women were classified as premenopausal if they were still menstruating and as postmenopausal if they had a natural menopause (no periods for at least a year) or bilateral oophorectomy. Women with hysterectomy but without a bilateral oophorectomy were classified as postmenopausal if they were above the age of 56, and as premenopausal if they were below 43 years of age. Women who did not report menopausal status or had undergone hysterectomy without a bilateral oophorectomy and were aged 43–56 were classified as having "unknown" menopause status. Weekly servings of fruits and vegetables, total red meat intake, and total daily energy intake were derived from the 68-item modified version of the National Cancer Institute (NCI)–Block food frequency questionnaire administered to all participants at baseline (1995) and in the 2001 questionnaire [15]. Dietary variables were derived from the food frequency questionnaire administered in 1995 if the index period was prior to 2001 and from the 2001 food frequency questionnaire if the index period was at or after the 2001 follow-up. Time-varying covariates were reassigned for every 2 years of follow-up by using the Andersen-Gill data structure [16]. This creates a new record for every follow-up cycle at which the participant is at risk, and assigns covariate values for that specific questionnaire cycle. For adenoma cases in the nested case–control analysis, covariates were based on the questionnaires administered in the cycle prior to when the polyp (later determined to be an adenoma) was reported (index period). For matched controls, covariates were also based on responses in the questionnaire cycle before the "index period".

Statistical analysis

Baseline age-standardized means (continuous variables) and proportions (categorical variables) were calculated across baseline BMI categories for population characteristics. Anthropometric variables were analyzed as continuous (with effect estimates for adenoma and CRC risk per 1 standard deviation increase reported) and categorical variables. Tests for linearity assumption were conducted using restricted cubic spline regression for models with continuous anthropometric variables, and no deviations from linearity were observed for any anthropometric variable. WC, WHR, and ABSI were categorized in quintiles, BMI was categorized using World Health Organization recommended standardized categories (< 18.5, 18.5–24.9, 25–29.9, ≥ 30 kg/m^2), and weight gain since age 18 in 5 categories (< 10, 10–14, 15–19, 20–24, ≥ 25 lb). We used conditional logistic regression to estimate age-adjusted and multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for risk of colorectal adenoma in association with anthropometric factors. Associations between anthropometrics and colorectal cancer incidence were evaluated using Cox proportional hazards regression (PROC PHREG) using the Andersen-Gill data structure for time-varying exposures and covariates. Person-years were calculated from baseline until the occurrence of colorectal cancer, loss to follow-up, death, or the end of follow-up in 2011. Since colonoscopy screening may alter the natural history and subsequent risk of CRC through removal of preneoplastic adenomas, we conducted sensitivity analysis by excluding all cases of diagnosed adenomas in the CRC-anthropometrics analysis. In the multivariable models, we adjusted for the following potential confounders: age, education, smoking status, alcohol intake, family history of colorectal cancer in first-degree relative, regular aspirin use, menopausal status, vigorous activity, total energy intake, fruit and vegetable intake, and red meat intake. In addition, models with BMI and weight change since age 18 as the primary exposure variables adjusted for BMI at age 18. Models with WC or WHR as the exposure variables did not adjust for BMI because of the high correlation of BMI with these variables. Instead, ABSI was used as a measure of abdominal obesity uncorrelated with BMI. Tests for linear trend in models where anthropometric measures were treated as categorical variables were performed by assigning the median value for each category/quintile and modeling this variable as a continuous variable. To determine whether associations differed by age at diagnosis of adenoma or cancer ($<50, \geq 50$ years of age) we stratified primary analyses by age at diagnosis. For the CRC analysis (cohort), person-time contributed by the participants before they reached 50 years of age was the denominator for the CRC rates in the "< 50 years of age" stratum; and participants who did not develop cancer prior to 50 years of age were censored at age 50 for this stratum. Person-time was similarly calculated for the "≥ 50 years of age" stratum. We assessed effect modification of the association between adenoma and anthropometrics by age. Interaction was assessed using the log-likelihood ratio test that compared models with and without the multiplicative interaction terms of anthropometric factor with age category (e.g., BMI*age). In addition, we analyzed adenoma and cancer location within the colorectum—colon (proximal and distal) and rectal adenoma/cancer in separate models to determine site-specific associations of anthropometric factors with adenoma/cancer risk. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results

The baseline characteristics of the study population are shown in Table 1. At baseline, women in the highest categories of BMI were more likely to be postmenopausal and had lower educational attainment, less vigorous physical activity, greater total energy intake and servings per week of red meat, and a higher prevalence of regular aspirin use.

Adenoma

Overall, ORs for colorectal adenoma were not meaningfully different from 1.0 for categories of increasing BMI, waist circumference, and waist-to-hip ratio. Among women who gained 10 kgs or more since age 18, risk of adenoma was significantly increased compared to those with less than a 10 kg weight gain. Similarly, adenoma risk was higher with increasing ABSI even though the findings were not statistically significant. (Table 2) In models stratified by age (< 50, ≥ 50 years at diagnosis), associations of all anthropometric factors, except ABSI, were stronger in women with an older age of onset than younger women. One standard unit increase in BMI, waist circumference, and weight change since age 18 were associated with a 12%, 17%, and 8% increased risk of colorectal adenoma among older women whereas among women diagnosed before age 50 the corresponding ORs were below 1.0. Among the older women, a weight gain of 25 kg or more since age 18 relative to < 10 kgs was associated with a 38% increase in risk of adenoma (95% CI 1.03–1.86). However, no significant statistical interaction by age was observed for any anthropometric factor. (Table 2).

Analyses of anthropometric factors in relation to colon adenoma risk by site (proximal) are shown in Table 3. Limited numbers of rectal adenomas among older women in the analytic cohort resulted in unstable effect estimates and these results are not presented. Evidence of an association with measures of body size was observed for proximal adenoma risk. Although not shown, these associations were not observed for distal adenomas. One standard deviation increase in BMI was associated with a 14% increased risk of proximal adenoma (OR 1.14, 95% CI 1.00, 1.31) in women ≥ 50 years. Increasing waist circumference and waist-to-hip ratio were associated with a 35% (95% CI 1.12, 1.63) and 25% (95% CI 0.93, 1.68) increased risk of proximal adenomas with one SD increase, respectively. The association of weight gain since age 18 was also associated with proximal adenoma risk with a 25 kg weight gain (relative to < 10 kg weight gain) resulting in a 66% increased proximal adenoma risk (95% CI 1.13, 2.44) but not distal adenoma risk. Increasing ABSI also appeared to be associated with proximal adenoma risk (OR 1.88, 95% CI 0.99, 3.56 comparing the highest to the lowest quintile).

Colorectal cancer risk (CRC)

A total of 57,386 participants were included in the analysis after excluding those who had not returned any follow-up questionnaire or who had prevalent cancer at baseline. In the 16 years of follow-up from 1995 to 2011, 413 incident CRC cases were identified over 802,783 person-years. In multivariate models, none of the anthropometric factors were associated with CRC risk among either < 50 or ≥ 50 year old women (Table 4). Associations of anthropometric factors with CRC risk did not differ materially across sites (proximal, distal, rectal) and the results were mostly null (data not shown). In sensitivity analyses where all diagnosed cases of adenomas were excluded from the cohort, the primary associations between anthropometric factors and CRC risk remain unchanged (data not shown).

Discussion

Overall BMI and other anthropometric factors were not associated with the risk of either colorectal adenoma or cancer n this cohort study of Black women in the US. BMI, waist circumference, WHR, weight gain since age 18, and ABSI were modestly associated with increased risk of proximal colon adenomas, among women ≥ 50 years old. However,

Table 1 Baseline Characteristics in the Black Women's Health Study Cohort according to BMI, 1995

Variable	BMI < 18.5 (*n* = 932)		BMI 18.5–24.9 (*n* = 20,917)		BMI 25–29.9 (*n* = 17,854)		BMI ≥ 30 (*n* = 17,144)	
	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)	Mean (SD)	*n* (%)
Age, years; mean (SD)	31.76 (8.70)		36.19 (10.01)		40.36 (10.83)		40.52 (10.57)	
Education								
≤ 12 years		134 (14.41)		2972 (14.23)		3621 (20.32)		4084 (23.87)
13–15 years		364 (39.14)		7193 (34.45)		6458 (36.24)		6468 (37.80)
≥ 16 years		432 (46.45)		10,715 (51.32)		7743 (43.45)		6559 (38.33)
Current smokers		161 (17.27)		3182 (15.24)		3135 (17.59)		2695 (15.74)
Alcohol (≥ 7 drinks/week)		47 (5.06)		1138 (5.48)		1100 (6.21)		947 (5.57)
Family history of colorectal cancer in first-degree relative		34 (3.65)		1036 (4.95)		1027 (5.75)		1056 (6.16)
History of colorectal cancer screening		34 (3.65)		1269 (6.07)		1672 (9.36)		1533 (8.94)
Regular aspirin use		48 (5.15)		1424 (6.81)		1757 (9.84)		2082 (12.14)
Vigorous physical activity (≥ 5 h/week)		97 (10.71)		3706 (18.29)		2342 (13.71)		1408 (8.57)
Postmenopausal		59 (6.43)		2322 (11.63)		3597 (21.74)		3636 (22.93)
Postmenopausal hormone therapy (current)		28 (3.06)		1560 (7.59)		2071 (11.84)		1889 (11.26)
Total energy intake (kcal); mean (SD)	1530.73 (678.32)		1414.27 (606.93)		1447.86 (607.60)		1571.56 (647.91)	
Red meat servings/week; mean (SD)	4.61 (5.14)		3.49 (4.11)		3.77 (4.17)		4.61 (4.86)	
Fruit and vegetable servings/week; mean (SD)	12.50 (13.66)		14.43 (13.27)		15.58 (13.69)		15.11 (13.61)	

BMI body mass index, *SD* standard deviation

none of the selected anthropometric factors were associated with CRC risk in either young or old onset CRC. Our findings suggest that among African American women, obesity may be associated with adenoma risk among older but not younger women and that obesity is not associated with CRC risk.

Although it has been well established in studies largely comprising White participants that BMI modestly increases the risk of colorectal adenomas [1, 2], more so among men than women, studies in African Americans are limited, and there is a particular lack of data on adenoma risk in African American women. Data on anthropometric measures other than BMI are even more limited. Our findings are similar to those from two prospective colonoscopy-based studies. Sedjo et al. reported BMI and weight gain but not WC or WHR associated with adenoma risk [17]. Race-stratified results for BMI reported by Sedjo et al. suggested similar results among Whites and African Americans, but were underpowered for associations among African Americans. Murphy et al. in a colonoscopy-based study reported a

Table 2 Associations of anthropometric measures with incident colorectal adenoma by age in the Black Women's Health Study (in a nested matched case–control study[a]), 1997–2011

Anthropometrics	All Participants		< 50 years		≥ 50 years	
	# Cases/controls	Multivariate OR[b] (95% CI)	# Cases /controls	Multivariate OR[b] (95% CI)	# Cases /controls	Multivariate OR[b] (95% CI)
BMI (kg/m^2)						
Categories[c]						
< 18.5	3/12	0.56 (0.15, 2.09)	0/2	–	3/10	0.71 (0.18, 2.77)
18.5–24.9	209/617	1.00	74/187	1.00	135/430	1.00
25–29.9	332/993	1.01 (0.82, 1.24)	78/244	0.85 (0.58, 1.26)	254/749	1.09 (0.85, 1.40)
≥ 30	402/1200	1.06 (0.85, 1.32)	108 /340	0.91 (0.60, 1.37)	294/860	1.15 (0.88, 1.50)
P_{trend}[d]		0.70		0.60		0.39
Continuous						
1 SD (6.64 kg/m^2) increase[e]	–	1.05 (0.96, 1.16)	–	0.91 (0.79, 1.05)	–	1.12 (0.99, 1.24)
P, interaction by age[f]						0.08
Waist circumference (cm)						
Quintiles[c]						
< 76.2	164/474	1.00	56/160	1.00	108/314	1.00
76.2–88.8	150/481	0.91 (0.70, 1.19)	42/128	0.97 (0.60, 1.58)	108/353	0.92 (0.67, 1.26)
88.9–99.0	147/425	1.00 (0.74, 1.36)	42/120	0.92 (0.52, 1.63))	105/305	1.06 (0.67, 1.26)
99.1–109.1	143/453	0.96 (0.69, 1.34)	32/115	0.75 (0.39, 1.42)	111/338	1.09 (0.73, 1.61)
≥ 109.2	171/411	1.20 (0.84, 1.71)	36/107	0.89 (0.45, 1.75)	135/304	1.38 (0.90, 2.10)
P_{trend}[d]		0.36		0.57		0.13
Continuous						
1 SD (18.23 cm) increase[e]	–	1.09 (0.97, 1.23)	–	0.94 (0.75, 1.17)	–	1.17 (1.01, 1.35)
P, interaction by age[f]						0.11
Waist-to-hip ratio						
Quintiles[c]						
< 0.75	142/471	1.00	40/139	1.00	102/332	1.00
0.75–0.82	167/432	1.30 (0.99, 1.71)	48/113	1.83 (1.09, 3.11)	119/319	1.21 (0.88, 1.68)
0.83–1.07	138/433	1.03 (0.74, 1.34)	33/128	1.08 (0.60, 1.96)	105/305	1.05 (0.72, 1.52)
1.08–1.23	168/456	1.18 (0.65, 1.70)	44/113	2.42 (0.76, 7.72)	124/343	0.99 (0.54, 1.81)
≥ 1.24	157/432	1.19 (0.58, 1.54)	41/123	2.20 (0.65, 7.43)	116/309	1.03 (0.56, 1.88)
P_{trend}[d]		0.54		0.41		0.51
Continuous						
1 SD (0.25) increase[e]	–	1.02 (0.84, 1.24)	–	0.91 (0.61, 1.34)()	–	1.06 (0.84, 1.34)
P, interaction by age[f]						0.50
Weight change since age 18, kg						
Categories[c]						
< 10	128/450	1.00	41/147	1.00	87/303	1.00
10–14	121/327	1.37 (1.02, 1.85)	41/104	1.35 (0.79, 2.29)	80/223	1.41(0.98, 2.04)
15–19	121/397	1.11 (0.83, 1.49)	36/91	1.34 (0.79, 2.29)	85/306	1.07 (0.75, 1.52)
20–24	176/411	1.58 (1.20, 2.09)	46/104	1.60 (0.96, 2.67)	130/307	1.65 (1.18, 2.31)
≥ 25	397/1,217	1.26 (1.00, 1.60)	96/323	1.05 (0.68, 1.63)	301/894	1.38 (1.03, 1.86)
P_{trend}[d]		0.11		0. 93		0.04

Table 2 (continued)

Anthropometrics	All Participants		< 50 years		≥ 50 years	
	# Cases/controls	Multivariate OR[b] (95% CI)	# Cases /controls	Multivariate OR[b] (95% CI)	# Cases /controls	Multivariate OR[b] (95% CI)
Continuous						
1 SD (15.41 kg) increase[e]	–	1.05 (0.97, 1.14)	–	0.98 (0.86, 1.16)	–	1.08 (0.98, 1.18)
P, interaction by age[f]						0.43
Body shape index (ABSI)						
Quintiles[c]						
< 0.065	132/446	1.00	47/145	1.00	85/301	1.00
0.065–0.071	156/445	1.14 (0.86, 1.50)	46/136	0.92 (0.55, 1.54)	110/309	1.45 (0.89, 2.36)
0.072–0.080	156/446	1.16 (1.86, 1.58)	43/135	1.02 (0.57, 1.83)	113/311	0.90 (0.65, 1.25)
0.081–0.089	154/445	1.26 (0.84, 1.89)	35/107	1.13 (0.50, 2.56)	119/338	0.94 (0.71, 1.26)
≥ 0.090	173/445	1.44 (0.95, 2.18)	36/103	1.40 (0.61, 3.23)	137/342	0.60 (0.29, 1.23)
P_{trend}[d]		0.09		0.47		0.14
Continuous						
1 SD (0.01) increase[e]		1.07 (0.93, 1.23)	–	1.06 (0.80, 1.42)	–	1.06 (0.90, 1.26)
P, interaction by age[f]						0.93

OR odds ratio, *CI* confidence interval

[a]Cases and controls were matched on age and follow-up time

[b]Adjusted for age, education, smoking, alcohol intake, family history of CRC in a first-degree relative, NSAID use, total energy intake, red meat intake, fruit and vegetable intake, menopausal status, and physical activity

[c]Based on a conditional logistic regression model with anthropometric exposures modeled as categorical variables

[d]P_{trend} assessed by χ^2 test for linear trend

[e]Based on a conditional logistic regression model with anthropometric exposures modeled as continuous variables

[f]Calculated using the likelihood ratio test comparing the fit of a model including the cross-product term between the anthropometric variable (e.g., BMI) and age category to a model without the cross-product term (e.g., BMI*age category)

moderate increase in adenoma risk associated with increasing WC and WHR but not BMI among African American men and women [18]. Our results for BMI and adenoma risk among older women are similar to estimates from meta-analyses based largely on white women [1, 2]. Our results for WHR conform to previously reported estimates of WHR-associated adenoma risks [19, 20], but only for proximal adenomas, that suggested WHR as an independent risk factor for adenoma among older women. Multiple studies have reported higher prevalence of proximal adenomas among African Americans compared to Caucasians and other races [21–23], but the reasons for this observation remain unclear. Given the high rates of obesity in African American women compared to other races [24], our findings that obesity is an independent risk factor for proximal adenomas might partly explain the higher prevalence of proximal adenomas in this population.

Most studies of BMI in relation to CRC risk have been conducted in primarily White populations. Results from these studies are conflicting, with some suggesting multiple anthropometric factors, including BMI, associated with CRC risks [25–27]; others suggesting markers of abdominal obesity but not BMI as CRC risk factors [28, 29]; and, still others reporting no association between anthropometrics and CRC risk [30–34]. Analyses among postmenopausal women in the Women's Health Initiative [25] (BMI, WC, WHR, and ABSI), Cancer Prevention Study–II cohort [26] (BMI and WC), and the Nurses' Health Study [27] (BMI, WC, and WHR) reported positive associations of BMI and other anthropometric factors with CRC risk. However, in a pooled analysis of 11 Australian cohorts, Harding et al. reported modest CRC risk associated with WC, WHR, and ABSI but not BMI [28]; and results from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort suggested that abdominal obesity measures (WC and WHR) but not BMI were associated with colon cancer risk among women [29]. In a more recent analysis from the EPIC cohort, Steins Bisschop et al. reported that neither BMI nor weight gain were associated with CRC risk among women [31]. Other large studies of White women have reported results

Table 3 Associations of anthropometric measures with incident colon adenoma by site among ≥ 50 year old women in the Black Women's Health Study (in a nested matched case–control study[a]), 1997–2011

Anthropometrics	All Colon adenoma		Proximal colon adenoma	
	# Cases/controls	Multivariate OR[b] (95% CI)	# Cases/controls	Multivariate OR[b] (95% CI)
BMI (kg/m^2)				
Categories[c]				
< 18.5	2/9	0.50 (0.10, 2.45)	0/9	–
18.5–24.9	123/385	1.00	88/385	1.00
25–29.9	227/680	1.04 (0.80, 1.36)	156/680	1.08 (0.79, 1.47)
≥ 30	273/788	1.14 (0.86, 1.51)	197/788	1.13 (0.81, 1.58)
P_{trend}[d]		0.45		0.76
Continuous				
1 SD (6.64 kg/m^2) increase[e]	–	1.08 (0.96, 1.21)	–	1.14 (1.00, 1.31)
Waist circumference (cm)				
Quintiles[c]				
< 76.2	95/281	1.00	58/182	1.00
76.2–88.8	98/318	0.94 (0.67, 1.31)	66/225	0.98 (0.64, 1.49)
88.9–99.0	94/269	1.11 (0.75, 1.63)	70/184	1.39 (0.86, 2.26)
99.1–109.1	103/312	1.12 (0.74, 1.7)	68/228	1.17 (0.7, 1.98)
≥ 109.2	126/284	1.41 (0.9, 2.21)	100/206	1.92 (1.11, 3.33)
P_{trend}[d]		0.13		0.03
Continuous				
1 SD (18.23 cm) increase[e]	–	1.17 (1.00, 1.36)	–	1.35 (1.12, 1.63)
Waist-to-hip ratio				
Quintiles[c]				
< 0.75	92/296	1.00	51/195	1.00
0.75–0.82	107/283	1.2 (0.85, 1.7)	76/187	1.57 (1.02, 2.44)
0.83–1.07	93/272	1.01 (0.68, 1.49)	63/183	1.32 (0.8, 2.17)
1.08–1.23	114/319	0.97 (0.52, 1.83)	87/248	1.36 (0.63, 2.95)
≥ 1.24	109/288	1.06 (0.57, 2)	84/208	1.66 (0.76, 3.62)
P_{trend}[d]		0.71		0.12
Continuous				
1 SD (0.25) increase[e]	–	1.08 (0.85, 1.37)	–	1.25 (0.93, 1.68)
Weight change since age 18 (kg)				
Categories[c]				
< 10	79/275	1.00	50/191	1.00
10–14	74/198	1.45 (0.99, 2.13)	47/140	1.44 (0.89, 2.31)
15–19	75/281	1.01 (0.7, 1.47)	57/197	1.22 (0.78, 1.91)
20–24	116/280	1.61 (1.13, 2.3)	79/201	1.78 (1.15, 2.75)
≥ 25	278/814	1.39 (1.02, 1.89)	206/574	1.66 (1.13, 2.44)
P_{trend}[d]		0.05		0.01
Continuous				
1 SD (15.41 kg) increase[e]	–	1.07 (0.97, 1.18)	–	1.12 (1.00, 1.26)
Body shape index (ABSI)				
Quintiles[c]				
< 0.065	75/265	1.00	47/179	1.00
0.065–0.071	101/282	1.24 (0.87, 1.75)	66/196	1.3 (0.84, 2.01)
0.072–0.080	101/279	1.28 (0.87, 1.89)	73/189	1.57 (0.96, 2.55)
0.081–0.089	112/311	1.36 (0.83, 2.24)	81/223	1.59 (0.86, 2.95)
≥ 0.090	125/314	1.52 (0.9, 2.56)	93/229	1.88 (0.99, 3.56)
P_{trend}[d]		0.12		0.05

Table 3 (continued)

Anthropometrics	All Colon adenoma		Proximal colon adenoma	
	# Cases/controls	Multivariate OR[b] (95% CI)	# Cases/controls	Multivariate OR[b] (95% CI)
Continuous				
1 SD (0.01) increase[e]	–	1.06 (0.89, 1.27)	–	1.14 (0.91, 1.41)

CRC colorectal cancer, *OR* odds ratio, *CI* confidence interval

[a]Cases and controls were matched on age and follow-up time

[b]Adjusted for age, education, smoking, alcohol intake, family history of CRC in a first-degree relative, NSAID use, total energy intake, red meat intake, fruit and vegetable intake, menopausal status, and physical activity

[c]Based on a conditional logistic regression model with anthropometric exposures modeled as categorical variables

[d]P_{trend} assessed by χ^2 test for linear trend

[e]Based on a conditional logistic regression model with anthropometric exposures modeled as continuous variables

similar to our own. In an analysis from the Framingham Heart Study, BMI and waist circumference were not associated with colon cancer risk among women [30]. Similarly, Keimling et al. reported null associations between BMI, WHR, and WC and CRC risk among women in the NIH-AARP cohort [32], and Renehan et al. reported no associations between BMI at age 18 and weight change since age 18 with CRC risk among women in this cohort [33]. Our results for young onset colorectal cancer among Black women are different from those observed in the Nurses' Health Study II. Liu et al. [35] reported a higher risk of CRC in a cohort of primarily White women comparing overweigh (BMI 25–29.9) and obese (BMI ≥ 30) women to those with BMIs between 18.5 and 24.9. However, BMI (and other anthropometric factors) were not associated with young onset CRC risk among Black women in our study.

Only one previous study has investigated risks of colorectal adenoma and CRC with anthropometric factors within the same study. In an analysis from the PLCO, in a primarily White population, Kitahara et al. reported that BMI was not associated with either adenoma or CRC risk among women [36]. That study lacked data on proximal adenomas because of the use of sigmoidoscopy for CRC screening in the PLCO and did not report on WC/WHR. Our study is the first among African Americans to investigate adenoma and CRC risk in the same study with data on both proximal and distal (although not shown) adenomas and cancer and to assess multiple anthropometric exposures. Our results for CRC are similar to those reported by Kitahara et al. [36] but in our study increasing BMI was associated with proximal colorectal adenoma risk among older women. Although CRCs usually arise from adenomatous polyps, most adenomas will not progress to cancer. Our finding that obesity, after adjusting for diet, physical activity, and other CRC risk factors, might be associated with adenoma but not CRC, suggests that obesity might be important for adenoma formation but not factors related to progression (e.g., dysplasia) to cancer among African American women.

The strengths of our study include the nested design for adenoma analysis within a large prospective cohort of African American women in the United States, adenoma and cancer outcomes verified by medical records, availability of data to derive multiple anthropometric exposures, high cohort retention resulting in updated measures of exposures and covariates, and detailed information on a large number of covariates. In addition, results from our study are generalizable to most African American women in the United States, but not to those with low educational attainment. More than 95% of the BWHS cohort had a high school education or more at enrollment compared with 83% of African American women in the general population [37].

Our study was limited by the use of self-reported data for anthropometrics. However, in a validation study of 115 BWHS participants from Washington DC area, Spearman correlations of self-reported anthropometric versus technician-measured data were > 0.90 for height and weight; and > 0.70 for WC [10]. Participant-reported polyps were verified by medical record review in our study, but the absence of polyps was not verified. Misclassification in which participants diagnosed with adenomas failed to report polyps and were therefore included in the control group would attenuate the anthropometrics–adenoma association toward null. However, previous studies have shown that self-report of polyps has a high negative predictive value (94%–100%) for adenomas, and it is unlikely that this was a major source of bias in our study [38, 39]. We had smaller sample sizes for analyses for CRC outcomes by age groups, i.e., < 50 or ≥ 50 years, and were underpowered for such analyses, especially for rectal cancer. Given the 5 anthropometric factors we examined including analyses stratified by age it is possible a few associations might have been statistically significant simply due to chance (multiple testing) and our findings from proximal adenomas should be validated in future studies. Similarly, we did not have adequate number of events or follow-up time to effectively determine risk of either adenoma or CRC associated with a very low BMI (< 18.5 kg/m^2). Finally, we

Table 4 Associations of anthropometric measures with incident colorectal cancer in the Black Women's Health Study 1995–2011

Anthropometrics	All participants		< 50 years		≥ 50 years	
	# Cases/person-years	Multivariate RR[a] (95% CI)	# Cases/person-years	Multivariate RR[a] (95% CI)	# Cases/person-years	Multivariate RR[a] (95% CI)
BMI (kg/m^2)						
Categories[b]						
< 18.5	3/7466	1.50 (0.47, 4.77)	0/6338	–	3/1128	2.18 (0.68, 7.00)
18.5–24.9	89/221,816	1.00	26/167,945	1.00	63/53,870	1.00
25–29.9	147/260,604	1.02 (0.77, 1.35)	46/163,148	1.46 (0.89, 2.38)	101/97,456	0.84 (0.61, 1.16)
≥ 30	172/308,962	0.99 (0.73, 1.33)	41/190,988	0.97 (0.55, 1.71)	131/117,974	0.90 (0.65, 1.26)
P_{trend}[c]		0.98		0.65		0.89
Continuous						
1 SD (6.64 kg/m^2) increase[d]	–	1.03 (0.90, 1.17)	–	0.88 (0.68, 1.12)	–	1.04 (0.90, 1.21)
P, interaction by age[e]						0.39
Waist circumference (cm)						
Quintiles[b]						
< 73	53/155,688	1.00	21/123,740	1.00	32/31,948	1.00
73–80	49/108,504	1.07 (0.71, 1.61)	14/78,883	0.92 (0.47, 1.82)	35/29,621	1.11 (0.69, 1.8)
81–90	94/149,791	1.24 (0.86, 1.78)	21/97,279	1.04 (0.56, 1.91)	73/52,513	1.25 (0.82, 1.9)
91–103	88/156,263	1.13 (0.78, 1.64)	26/93,404	1.28 (0.7, 2.35)	62/62,859	1.03 (0.67, 1.6)
≥ 104	75/132,762	1.12 (0.75, 1.70)	12/64,854	0.82 (0.37, 1.79)	63/67,908	1.13 (0.71, 1.81)
P_{trend}[c]		0.55		0.85		0.81
Continuous						
1 SD (18.23 cm) increase	–	1.04 (0.91, 1.18)	–	0.96 (0.75, 1.23)	–	1.02 (0.89, 1.18)
P, interaction by age[e]						0.71
Waist-to-hip ratio						
Quintiles[b]						
< 0.72	80/136,281	1.00	24/97,157	1.00	56/39,124	1.00
0.73–0.78	54/138,724	0.56 (0.39, 0.81)	11/96,567	0.45 (0.22, 0.92)	43/42,157	0.68 (0.46, 1.01)
0.79–0.85	78/135,689	0.87 (0.63, 1.20)	20/93,631	0.83 (0.46, 1.51)	58/42,058	0.91 (0.63, 1.32)
0.86–1.10	71/139,970	0.77 (0.55, 1.09)	23/93,372	0.96 (0.53, 1.75)	48/46,598	0.77 (0.52, 1.14)
≥ 1.11	71/136,856	0.72 (0.47, 1.08)	14/65,698	0.7 (0.3, 1.64)	57/71,158	0.75 (0.47, 1.19)
P_{trend}[c]		0.35		0.99		0.37
Continuous						
1 SD (0.25) increase[d]	–	0.91 (0.79, 1.05)	–	0.91 (0.68, 1.23)	–	0.92 (0.79, 1.08)
P, interaction by age[e]						0.16
Weight change since age 18 (kg)						
Categories[b]						
< 10	62/183,212	1.00	27/146,155	1.00	35/37,057	1.00
10–14	50/108,338	1.11 (0.75, 1.65)	8/77,856	0.47 (0.21, 1.03)	42/30,482	1.51 (0.96, 2.38)
15–19	71/110,772	1.37 (0.95, 1.96)	26/72,932	1.48 (0.85, 2.56)	45/37,840	1.31 (0.83, 2.05)
20–24	61/115,724	0.96 (0.65, 1.41)	16/72,117	0.86 (0.46, 1.61)	45/43,607	1.16 (0.74, 1.82)
≥ 25	159/275,918	1.11 (0.81, 1.53)	34/156,667	0.77 (0.45, 1.31)	125/119,252	1.25 (0.84, 1.85)
P_{trend}[c]		0.88		0.29		0.80

Table 4 (continued)

Anthropometrics	All participants		< 50 years		≥ 50 years	
	# Cases/person-years	Multivariate RR[a] (95% CI)	# Cases/person-years	Multivariate RR[a] (95% CI)	# Cases/person-years	Multivariate RR[a] (95% CI)
Continuous						
1 SD (15.41 kg) increase[d]	–	1.02 (0.92, 1.14)	–	0.89 (0.73, 1.09)	–	1.04 (0.92, 1.18)
P, interaction by age[e]						0.61
Body shape index (ABSI)						
Quintiles[b]						
< 0.065	73/139,890	1.00	18/97,488	1.00	55/42,402	1.00
0.065–0.068	67/139,682	1.02 (0.72, 1.43)	23/102,391	1.26 (0.68, 2.33)	44/37,291	0.91 (0.61, 1.35)
0.069–0.073	64/139,893	0.87 (0.61, 1.25)	17/100,549	0.93 (0.48, 1.8)	47/39,344	0.92 (0.62, 1.36)
0.074–0.082	77/139,927	0.94 (0.67, 1.33)	23/89,468	1.32 (0.7, 2.47)	54/50,459	0.85 (0.58, 1.24)
≥ 0.083	76/139,831	0.84 (0.57, 1.25)	13/66,162	0.89 (0.39, 2.02)	63/73,669	0.84 (0.55, 1.29)
P_{trend}[c]		0.36		0.99		0.37
Continuous						
1 SD (0.01) increase[d]	–	0.92 (0.81, 1.04)		0.96 (0.74, 1.23)		0.92 (0.80, 1.05)
P, interaction by age[e]						0.23

CRC colorectal cancer, *NSAID* nonsteroidal anti-inflammatory drug, *HRT* hormone replacement therapy, *RR* relative risk, *CI* confidence interval

[a]Adjusted for age, education, smoking, alcohol intake, family history of CRC in a first-degree relative, CRC screening, NSAID use, total energy intake, red meat intake, fruit and vegetable intake, menopausal status, and physical activity

[b]Based on a Cox proportional regression model with anthropometric exposures modeled as categorical variables

[c]P_{trend} assessed by χ^2 test for linear trend

[d]Based on a Cox proportional regression model with anthropometric exposures modeled as continuous variables

[e]Calculated using the likelihood ratio test comparing the fit of a model including the cross-product term between the anthropometric variable (e.g., BMI) and age category to a model without this term (e.g., BMI*age category)

did not adjust for sedentary behavior, and control for vigorous activity and red meat, fruit, and vegetable intake might not have been adequate to prevent residual confounding by physical activity and diet.

In summary, BMI and other indicators of obesity were not associated with CRC risk or young onset CRC risk in this large cohort of African American women. However, BMI, waist circumference, WHR, and weight change were associated with moderately increased risk of proximal colorectal adenomas among African American women above the age of 50. More studies in minority populations are needed to firmly establish the role of obesity in CRC risk.

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