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Research Article

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Obesity and Prostate Cancer Aggressiveness among African and Caucasian Americans in a Population-Based Study

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Abstract

Background: This study evaluated obesity and prostate cancer aggressiveness relationship in a population-based incident prostate cancer study.

Methods: The North Carolina–Louisiana Prostate Cancer Project includes medical records data for classification of prostate cancer aggressiveness at diagnosis by using clinical criteria for 1,049 African American (AA) and 1,083 Caucasian American (CA) participants. An association between prostate cancer aggressiveness and obesity, measured using body mass indices (BMI) and waist-to-hip ratio (WHR), was assessed using ORs and 95% CIs adjusted for confounders.

Results: A significantly positive association was found between prostate cancer aggressiveness and obesity. The ORs for high aggressive prostate cancer among prediagnosis obese and severely obese were 1.48 (95% CI = 1.02–2.16) and 1.98 (95% CI = 1.31–2.97), respectively, compared with normal weight research subjects. Race-stratified results suggested the association is stronger among CAs. Interaction model showed that normal weight AAs had more aggressive prostate cancer than normal weight CAs (OR = 2.69, 95% CI = 1.36–5.30); severe obesity was associated with aggressive disease in AAs (OR = 3.90, 95% CI = 1.97–7.75). WHR > 0.98 among all research subjects adjusted for race was significantly associated with high aggressive prostate cancer (OR = 1.42, 95% CI = 1.00–2.00) when compared with WHR < 0.90. The stratified result is less clear among AAs.

Conclusions: This study shows a positive association between obesity and aggressive prostate cancer. AAs have more aggressive prostate cancer in general than CAs even at normal weight. Therefore, the association between obesity and aggressiveness is not as evident in AAs as in CAs.

Impact: This study provides a unique opportunity to examine impact of race on obesity and high aggressive prostate cancer relationship. *Cancer Epidemiol Biomarkers Prev; 20(5); 844–53. ©2011 AACR.*

Introduction

Obesity has been associated with increased risk of several types of cancer, including breast and colon cancer (1), but the relationship between obesity and prostate cancer is less clear. Giovannucci and colleagues reported a relationship between increased risk of fatal prostate cancer and taller height and higher body mass index (BMI), using results from the Health Professionals Follow-up Study (2). Findings from the Cancer Prevention Study II, another large prospective cohort study in the United States, suggested that obesity is positively associated with prostate cancer mortality (3). Recent study results from the Shared Equal Access Regional Cancer Hospital (SEARCH) database found that obesity is a risk factor for aggressive prostate cancer regardless of race (4). On the other hand, a cross-sectional evaluation of 1,814 prostate cancer patients in Germany suggested that obesity does not predispose to more aggressive prostate cancer either at biopsy or at radical prostatectomy (5). Similarly, a clinical cohort of 2,687 patients who underwent treatment for low and intermediate grade of prostate cancer found no association between BMI and biochemical failure after at least of 2-year follow-up (6). Another population-based cohort study of 10,564 men in Sweden suggested that height is associated with total and nonaggressive prostate cancer risk but not with aggressive cancer (7). BMI was not associated with either aggressive or nonaggressive prostate cancer. Review of published studies concluded that BMI is not associated

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with prostate cancer overall but may be associated with more aggressive disease (8–11).

A proposed mechanism for the obesity and prostate cancer aggressiveness association involves testosterone, estrogen, and the insulin-like growth factor I (IGF-I) axis. Specifically, men with excess central adiposity have lower testosterone levels, which may be associated with higher stage and grade of prostate cancer at the time of diagnosis (12, 13). In addition, circulating IGF-I, a potential prostate cancer mitogen, is elevated among men with hyperinsulinemia, which is common among obese men (14). The inconsistent study findings on prostate cancer and obesity may be explained, at least in part, by the high prevalence of latent prostate cancer and the widespread use of prostate-specific antigen (PSA) for screening for prostate cancer in the United States (15).

A closer look at the data reveals that the majority of the evidence for a relationship between obesity and advanced prostate cancer is based on Caucasian American (CA) populations and a greater burden of prostate cancer is seen in African Americans (AAs). Age-adjusted prostate cancer incidence and mortality rates for AA men are approximately 60% and 140% higher, respectively, than rates for CAs (16). Therefore, the purpose of this study was to evaluate the relationship between obesity, measured using BMI and waist-to-hip ratio (WHR), and prostate cancer aggressiveness classified on the basis of Gleason grade, clinical stage, and PSA at diagnosis in a population-based study of similar numbers of incident prostate cancer cases in African and CAs.

Materials and Methods

Data from the North Carolina–Louisiana Prostate Cancer Project (PCaP), a population-based cross-sectional study of incident prostate cancer in 2 southern states in the United States, was analyzed (17). Research subjects were identified using rapid case ascertainment to identify newly diagnosed prostate cancer cases in an unbiased fashion.

Analysis of the relationship between obesity and prostate cancer aggressiveness was based on research data collected from research subjects who were recruited from July 1, 2004, through August 31, 2009. Details of PCaP have been described (17). Briefly, PCaP is composed of investigators from 12 institutions across the country. Fieldwork was conducted in Louisiana and North Carolina by investigators and staff located at Louisiana State University Health Sciences Center and University of North Carolina at Chapel Hill.

Residents of the North Carolina and Louisiana study catchment areas with a first diagnosis of histologically confirmed adenocarcinoma of the prostate on or after July 1, 2004, were eligible to participate in the PCaP study if they were 40 to 79 years of age at diagnosis, could complete the study interview in English, did not live in an institution (nursing home), were not cognitively impaired or in a severely debilitated physical state, and were not under the influence of alcohol, severely medicated, or apparently psychotic at the time of the interview. Eligible men also must have self-identified as either AA/black or CA/white in response to the open-ended interview question "What is your race?" Research protocols were approved by the institutional review boards at UNC, LSUHSC, and Department of Defense Prostate Research Program. The participation rates of the PCaP were 62% in North Carolina, 63% in post–Hurricane Katrina Louisiana, and 73% in pre–Hurricane Katrina Louisiana.

Weight (in kg), height, and waist and hip circumference (in cm) were measured at the time of interview (median 118.5 days after prostate cancer diagnosis) by PCaP nurses by using standardized instruments. Participants were also asked about their usual weight and height at age 25 and their weight 1 year prior to the research study visit. Height and weight measurements taken at the time of interview and self-reported weight 1 year prior to the study visit were used to calculate 2 separate measures of BMI. Waist and hip circumferences measured at the time of interview were used to calculate the WHR.

PCaP nurses administered a series of structured questionnaires that solicited information on background characteristics, occupation, family history of prostate cancer, comorbid conditions, health care access, prostate cancer diagnosis and screening history, diet, supplement use, physical activity, and other characteristics. Participants also were asked whether they or their doctor had decided which type of treatment was best for them and whether the treatment had started. Medical records related to prostate cancer diagnosis and staging were requested from the diagnosing physician of consenting participants and abstracted to obtain clinical stage, Gleason grade, and PSA at the time of diagnosis, in addition to other information. Approximately 10% of medical records were selected at random and abstracted by a second staff member to assess consistency among abstractors (18).

Complete prostate cancer aggressiveness data were available for 2,173 eligible research subjects. Standing height of 19 research subjects could not be measured because of their physical condition (could not stand) at interview, so they were excluded from further analysis because BMI could not be calculated. Two additional research subjects had questionable weight measurements at interview; another 20 research subjects did not remember their weight 12 months before prostate cancer diagnosis. Therefore, 41 (1.9%) research subjects were excluded from further analysis. Research subjects who were excluded were more likely to have high aggressive prostate cancer (3.8% vs. 1.5%, $P = 0.009$) and to be AAs (2.7% vs. 1.1%, $P = 0.006$). The remaining 2,132 research subjects were categorized as underweight (BMI <18 kg/m^2), normal weight (BMI $\geq$18 kg/m^2 and <25 kg/m^2), overweight (BMI $\geq$25 kg/m^2 and <30 kg/m^2), obese (BMI $\geq$30 kg/m^2 and <35 kg/m^2), or severely obese (BMI $\geq$35 kg/m^2). A total of 1,425 research subjects (74.6%) were

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categorized in the same weight category on the basis of the self-reported weight and weight measured at time of interview; 15 research subjects (0.7%) were categorized more than 1 weight category difference. Because the number of research subjects who were categorized as underweight was small (8 based on BMI 1-year before diagnosis and 19-based on postdiagnosis measurement), these research subjects were excluded from multivariate logistic regression models examining the association between BMI and prostate cancer aggressiveness. Results were reported on the basis of BMIs calculated from both self-reported weight and interviewer-measured weight. Waist and hip circumferences were not available for 2 additional research subjects who had BMI data. Therefore, 2,130 research subjects were included in the modeling of WHR and prostate cancer aggressiveness. WHR were categorized into 3 categories, where the reference category was defined as 0.90 or less using the World Health Organization's definition for metabolic syndrome for men (19). Those research subjects who had a WHR greater than 0.98 (upper tertile) were categorized as obese.

Cases were classified using Gleason grade, clinical stage, and PSA at diagnosis (17) as (i) high aggressive (Gleason sum $\geq$8, or PSA >20 ng/mL, or Gleason sum $\geq$7 and clinical stage T3–T4), (ii) low aggressive (Gleason sum <7 and clinical stage T1–T2 and PSA <10 ng/mL), or (iii) intermediate aggressive (all other cases). Both χ^2 test and Student's t test were used to test for significant differences in demographic characteristics between races ($\alpha = 0.05$). Multivariate logistic regression adjusting for age at diagnosis, education level, study site, smoking status, first-degree family history of prostate cancer (yes/no), previous prostate cancer screening history (whether research subjects had more than 1 PSA or digital rectal examination for prostate cancer screening prior to 12 months before prostate cancer diagnosis), PSA screening frequency (the interval between first PSA screening and cancer diagnosis in month divided by the number of PSA screenings), whether treatment of prostate cancer had started at time of interview, and Charlson comorbidity index (20, 21) was conducted to examine associations between obesity and prostate cancer aggressiveness. Sensitivity analyses were conducted using Gleason sum ($\geq$8 vs. <8) as an outcome variable to evaluate potential bias as the result of prostate cancer screening. Physical activity level [metabolic equivalent task (MET)/wk; refs. 22, 23], height, and type of prostate cancer treatment received were added to the model but did not impact the effect estimates (<10%) and were removed. Tests for interaction between race and BMI and WHR using continuous measures (both self-reported 12 months prior to diagnosis and measured at time of home interview after diagnosis) were conducted. Because the focus of this study was to examine the difference between races about obesity and prostate cancer aggressiveness, models were first presented pooled and stratified by race and then examined further using normal weight CAs as the reference group to examine the joint effect of race and obesity. Models also were evaluated after stratifying by prostate cancer screening history. Prostate cancer screening history did not seem to be an effect modifier. The values of $P < 0.05$ were considered statistically significant.

Results

Incident prostate cancer cases included 555 AAs and 563 CAs from Louisiana and 494 AAs and 520 CAs from North Carolina (Table 1). Average age at diagnosis was significantly higher for CAs than for AAs (64.2 and 61.8 years, respectively). Average height and BMI measured at interview were similar between CAs and AAs. However, AAs were more likely to be classified as obese or severely obese (43.9% vs. 37.9% based on self-reported and 39.0% vs. 37.6% measured at time of interview). In contrast, AAs had a slightly smaller mean WHR and were more likely to have WHR less than 0.90 than CAs.

Cigarette smoking differed between groups with 29.9% of AAs who reported having never smoked compared with 36.5% of CAs. Current smoking prior to prostate cancer diagnosis was twice as prevalent in AAs as CAs (25.0% vs. 11.4%). The average number of cigarettes smoked per day reported by smokers, however, was lower among AAs (17.8%) than CAs (24.2%). Education level also differed significantly between the groups: almost twice as many AAs than CAs reported education as less than high school graduate. Prostate cancer screening histories also differed; only 45.6% of AAs reported that they had ever been screened prior to diagnosis compared with 71.0% of CAs. Although tumor stage at prostate cancer diagnosis did not differ between African and CAs, AAs were more likely than CAs to be classified as having high aggressive (20.7% vs. 15.1%) or intermediate aggressive (33.3% vs. 29.2%) prostate cancer at diagnosis.

In logistic regression models adjusted for race, obese and severely obese were statistically significantly associated with high aggressive prostate cancer. The ORs were similar, regardless of whether the BMI was calculated on the basis of self-reported preprostate cancer diagnosis body weight or body weight measured at the time of study interview after diagnosis. The ORs for high aggressive prostate cancer among obese were 1.48 (95% CI = 1.02–2.16) and 1.54 (1.07–2.21), and the ORs among severely obese were 1.98 (95% CI = 1.31–2.97) and 1.73 (95% CI = 1.14–2.61) for self-reported and interviewer-measured BMI, respectively. WHR greater than 0.98 was also significantly associated with high aggressive prostate cancer (OR = 1.42, 95% CI = 1.00–2.00) when compared with those whose WHR was less than 0.90.

Test for interaction between race and BMI using continuous measures (both self-reported 12 months prior to diagnosis and measured at time of home interview after diagnosis) were not statistically significant ($P = 0.194$ and $P = 0.156$, respectively). The P value of test for interaction between WHR and race was 0.002. Statistical models

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Table 1. Descriptive statistics on AAs and CAs with incident prostate cancer

	AAs ($N = 1,049$)	CAs ($N = 1,083$)	Difference testing/P[a]
Louisiana, *n*	555	563	
North Carolina, *n*	494	520	
	Mean (SD)		
Age, y	61.8 (7.8)	64.2 (7.9)	<0.0001
BMI, kg/m^2			
Self-report prior to diagnosis	29.9 (6.0)	29.5 (5.0)	0.097
Measured at interview	29.2 (5.8)	29.2 (4.9)	0.966
Height, cm	175.3 (7.3)	175.3 (6.9)	0.997
WHR	0.95 (0.06)	0.96 (0.06)	<0.0001
Cigarettes per day[b]	17.8 (26.5)	24.2 (18.8)	0.006
Gleason sum	6.6 (0.9)	6.5 (0.9)	0.013
PSA at diagnosis	17.8 (69.1)	12.4 (76.3)	0.084
	***n* (%)**		
Self-reported BMI[c]			
BMI <18 kg/m^2 Underweight	5 (0.5)	3 (0.3)	<0.0001
BMI 18–25 kg/m^2 Normal weight	197 (18.8)	151 (13.9)	
BMI >25–30 kg/m^2 Overweight	386 (36.8)	518 (47.8)	
BMI 30–35 kg/m^2 Obese	292 (27.8)	286 (26.4)	
BMI >35 kg/m^2 Severely obese	169 (16.1)	125 (11.5)	
Measured BMI			
BMI <18 kg/m^2 Underweight	14 (1.3)	5 (0.5)	<0.0001
BMI 18–25 kg/m^2 Normal weight	219 (20.9)	177 (16.3)	
BMI >25–30 kg/m^2 Overweight	407 (38.8)	494 (45.6)	
BMI >30–35 kg/m^2 Obese	258 (24.6)	294 (27.2)	
BMI >35 kg/m^2 Severely obese	151 (14.4)	113 (10.4)	
WHR[c]			
≤0.90	223 (21.3)	131 (12.1)	<0.0001
>0.90–0.98	499 (47.6)	551 (50.9)	
>0.98	325 (31.0)	401 (37.0)	
Missing	2 (0.2)	0	
Smoking status			
Never smokers	314 (29.9)	395 (36.5)	<0.0001
Past smokers	473 (45.1)	565 (52.2)	
Current smokers	262 (25.0)	123 (11.4)	
Education level			
Less than high school graduate	626 (59.7)	337 (31.1)	<0.0001
High school graduate or some college	356 (33.9)	520 (48.0)	
College graduate or more	67 (6.4)	226 (20.9)	
Aggressiveness of tumor on diagnosis[d]			
Low	483 (46.0)	603 (55.7)	<0.0001
Intermediate	349 (33.3)	316 (29.2)	
High	217 (20.7)	164 (15.1)	
PSA screening[e]	478 (45.6)	769 (71.0)	<0.0001
Tumor stage			
T1	568 (55.8)	600 (55.4)	0.53
T2	427 (40.7)	454 (41.9)	
T3–T4	19 (1.8)	18 (1.7)	
Missing	18 (1.7)	11 (1.0)	
Cancer treatments			
Has not started/watchful waiting	256 (24.4)	213 (19.7)	0.0001
Surgery	473 (45.1)	568 (52.5)	
Hormone	50 (4.8)	46 (4.3)	

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Table 1. Descriptive statistics on AAs and CAs with incident prostate cancer (cont'd)

	AAs (N = 1,049)	CAs (N = 1,083)	Difference testing/P[a]
Radiation	165 (15.7)	122 (11.3)	
Brachytherapy	76 (7.2)	83 (7.7)	
Others	29 (2.8)	51 (4.7)	

[a]Testing for difference between Americans and CAs, using t test, for continuous variable and χ^2 test, for categorical variables.
[b]One AA research subject did not respond to smoking questions.
[c]Three AA and 1 CA research subjects did not report on weight 1-year prior to prostate cancer diagnosis, and 1 AA research subject did not have WHR measurement.
[d]Cases are classified as having low aggressive (Gleason score <7, stage ≤T2, PSA <10 ng/mL), high aggressive (Gleason score ≥8; PSA ≥20 ng/mL; or Gleason score = 7 if stage ≥T3), or intermediate aggressive prostate cancer (all others).
[e]PSA screening was defined to have occurred if research subjects had undergone more than 1 PSA or digital rectal examination for prostate cancer screening not counting those within 12 months prior to prostate cancer diagnosis.

were stratified further by race to examine the difference between races about obesity and prostate cancer aggressiveness. Obesity (OR = 2.86, 95% CI = 1.47–5.57) and severe obesity (OR = 3.44, 95% CI = 1.66–7.16) in research subjects 1 year prior to diagnosis (based on self-reported weight and measured height), compared with normal BMI, was associated with high aggressive prostate cancer among CAs after adjusting for confounders (Table 2). Although less pronounced, this relationship also was evident among CAs for BMI based on weight and height measured at the research study home visit after the diagnosis (OR = 2.00, 95% CI = 1.13–3.54) for obese; OR = 2.09, 95% CI = 1.06–4.14 for severe obese). The relationship was not as strong among AAs, but,

Table 2. ORs for the risk of greater aggressiveness as a function of BMI and WHR

	CAs		AAs		Both races[a]
	Aggressive[b]	OR (95% CI)	Aggressive[b]	OR (95% CI)	OR (95%CI)
BMI 1 y ago based on self-reported weight[c]					
Normal	13/138	1.00 Referent	46/151	1.00 Referent	1.00 Referent
Overweight	66/452	1.61 (0.85–3.05)	69/317	0.90 (0.58–1.40)	1.05 (0.74–1.46)
Obese	54/232	2.86 (1.47–5.57)	57/235	1.11 (0.69–1.79)	1.48 (1.02–2.16)
Severely obese	31/94	3.44 (1.66–7.16)	44/125	1.62 (0.97–2.72)	1.98 (1.31–2.97)
Test for trend		<0.0001		0.038	<0.0001
BMI after diagnosis based on measured weight[d]					
Normal	20/157	1.00 Referent	46/173	1.00 Referent	1.00 Referent
Overweight	65/429	1.27 (0.73–2.19)	78/329	1.13 (0.74–1.74)	1.13 (0.81–1.58)
Obese	56/238	2.00 (1.13–3.54)	52/206	1.38 (0.85–2.23)	1.54 (1.07–2.21)
Severely obese	23/90	2.09 (1.06–4.14)	37/114	1.71 (1.00–2.90)	1.73 (1.14–2.61)
Test for trend		0.004		0.032	0.001
WHR after diagnosis[d]					
<0.90	15/116	1.00 Referent	46/177	1.00 Referent	1.00 Referent
0.90–0.98	57/494	0.84 (0.45–1.57)	99/400	0.98 (0.65–1.47)	0.87 (0.62–1.22)
>0.98	92/309	2.03 (1.10–3.74)	72/235	1.18 (0.76–1.83)	1.42 (1.00–2.00)
Test for trend		<0.0001		0.413	0.005

[a]Model further adjusted for race.
[b]Number of cases was classified as having high aggressive prostate cancer versus low and intermediate aggressive prostate cancer.
[c]BMI was calculated on the basis of the height measured at the time of PCaP interview after prostate cancer diagnosis and weight from the self-reported weight 1 year prior to the PCaP interview.
[d]Weight, height, and waist and hip circumferences were measured at the time of PCaP interview after prostate cancer diagnosis by using a standard protocol.

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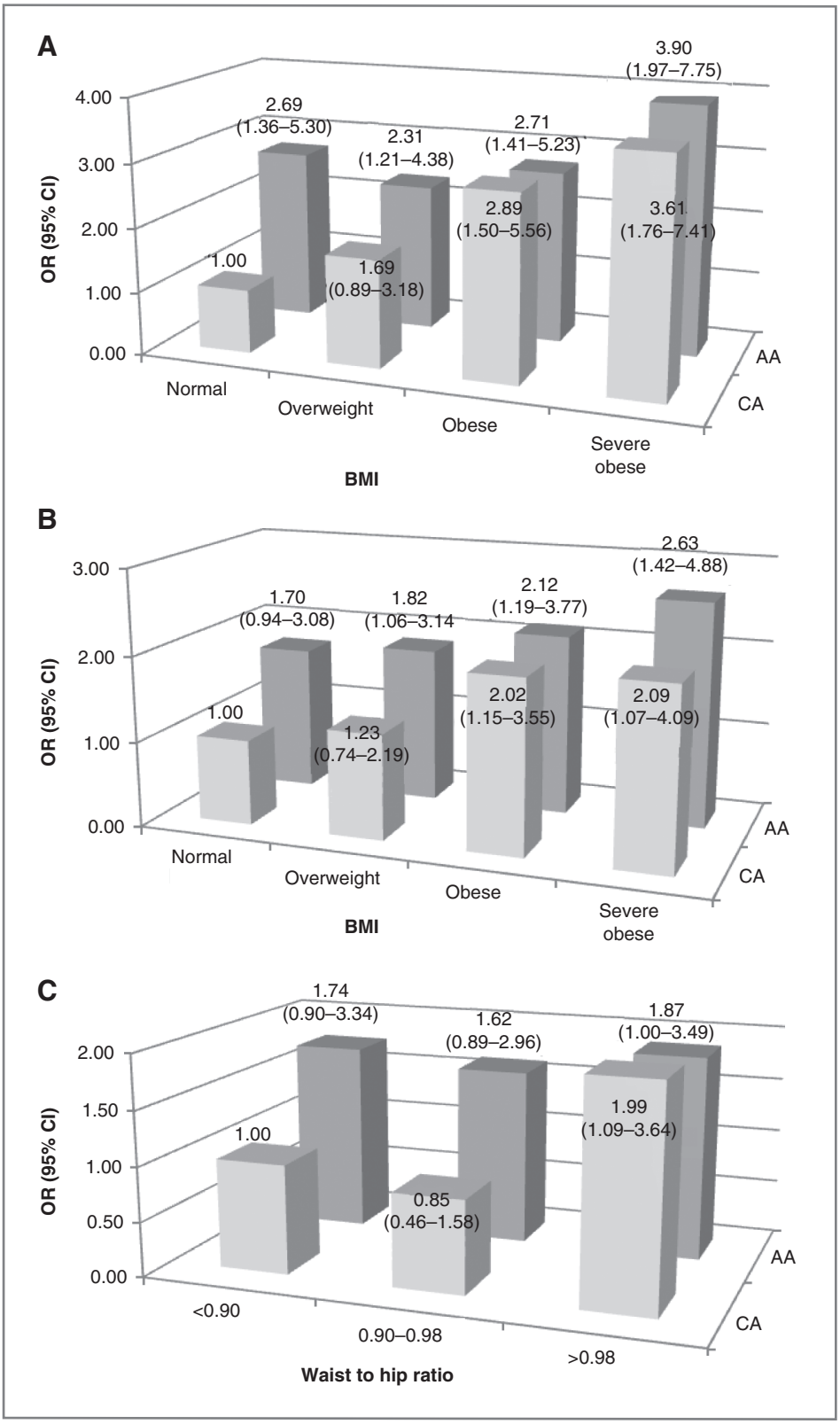

Figure 1. ORs and 95% CIs for the risk of greater aggressiveness as a function of BMI and WHR by race. A, ORs of high aggressiveness and prediagnosis self-reported BMI. B, ORs of high aggressiveness and BMI measured at PCaP interview. C, ORs of high aggressiveness and WHR measured at PCaP interview.

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consistent with the findings among CAs, severe obesity was associated with high aggressive prostate cancer among AAs, when based on BMI measured at time of interview (OR = 1.71, 95% CI = 1.00–2.00). The ordinal trend for increased obesity and OR for aggressive prostate cancer was statistically significant regardless of race or source of height and weight used to determine BMI. A difference in the magnitude of association by race was also seen for the highest tertiles of WHR when compared with the WHO recommendation. The adjusted OR for high WHR was 2.03 (95% CI = 1.10–3.74) among CAs compared with 1.18 (95% CI = 0.76–1.84) among AAs.

To further quantify the effects of race and obesity relative to a common referent group, normal BMI CAs were used as the reference group to examine the relationship between BMI and prostate cancer aggressiveness. Similar to the results observed in Table 2, obesity in CAs was associated with high aggressive prostate cancer on the basis of self-reported (OR = 3.61, 95% CI = 1.76–7.41) and interviewer-measured (OR = 2.09, 95% CI = 1.07–4.09) BMI (Fig. 1). Compared with the normal BMI CAs, normal BMI AAs were significantly more likely to have a diagnosis of high aggressive prostate cancer and the magnitude of this association was similar to that of obese CAs. OR was 2.69 (95% CI = 1.36–5.30) for precancer self-reported weight and OR was 1.70 (95% CI = 0.94–3.08) for weight measured at interview after cancer diagnosis. Although self-reported obesity was not significantly associated with high aggressive prostate cancer when normal weight AAs were used as the reference group, the interactive model using normal weight CAs as the referent showed that self-reported overweight and obesity were significantly associated with prostate cancer aggressiveness in each group. The ORs for high aggressive prostate cancer were 2.31 (95% CI = 1.21–4.38) for overweight (2.71, 95% CI = 1.41–5.23 for obese; 3.90 (95% CI = 1.97–7.75 for severely obese AAs). A similar finding was observed when examining the association based on the interviewer-measured BMI after cancer diagnosis. The association comparing normal weight AAs was not statistically significant when compared with normal weight CAs. WHR greater than 0.98 was significantly associated with high aggressive prostate cancer in both Caucasian (OR = 1.99, 95% CI = 1.09–3.64) and African (OR = 1.87, 95% CI = 1.00–3.49) Americans compared with CAs with WHR less than 0.90.

Polytomous models were used to estimate associations with intermediate and high aggressive prostate cancer compared with low aggressive prostate cancer. Relations between BMI or WHR and aggressiveness were limited to high aggressive prostate cancer (data not shown). The association between obesity and intermediate aggressive tumors was not significant. Sensitivity analyses conducted using high-grade prostate cancer (Gleason sum $\geq$8) as the outcome instead of high aggressive prostate cancer produced similar results (data not presented).

Discussion

Associations between measures of obesity and prostate cancer aggressiveness were examined using data from a population-based study of incident prostate cancer among AAs and CAs in Louisiana and North Carolina. A strong association between BMI and prostate cancer aggressiveness with a positive dose–response relationship was evident. WHR greater than 0.98 also was positively associated with high aggressive prostate cancer. The stratified results suggest the risk of developing high aggressive prostate cancer among obese and severely obese CAs is more than double that of normal weight CAs. AAs were more likely to have aggressive prostate cancer, even with normal BMI, than normal weight CAs. Although the trend for increased BMI and prostate cancer aggressiveness was not as clear among AAs as CAs, obese and severely obese AAs seem to have a diagnosis of more aggressive prostate cancer than leaner individuals. A stronger association was found using self-reported body weight prior to cancer diagnosis than body weight measured by a PCaP nurse after a prostate cancer diagnosis among Caucasians; but the postdiagnosis measurements were greater among AAs. The difference observed could be attributed to weight loss as the result of prostate cancer, treatment of prostate cancer, recall bias, differences in weight sensitivity, lack of knowledge of weight, or all of above. Nevertheless, obesity measured by either pre or postdiagnosis body weight showed significant association with prostate cancer aggressiveness.

Several studies have reported a positive association between obesity in adulthood and advanced prostate cancer and prostate cancer mortality (8), but other studies observed inverse associations between obesity early in life and aggressive disease (24, 25). This evidence carries weight on the basis of studies in which 80% or more of these research subjects were CAs (9, 26, 27). Most studies examining obesity and prostate cancer have included race as a confounder if AAs were included in the studies (28–32). Recently, analysis of the Shared Equal Access Regional Cancer Hospital (SEARCH) database (662 AA and 753 CA prostate cancer patients choosing radical prostatectomy) found that obesity was associated with greater risk of recurrence among both AAs and CAs (4). Authors conducted the analysis stratified by race and concluded that obesity was a risk factor for aggressive prostate cancer regardless of race (33, 34). Similar to these reports, the analysis reported herein took advantage of a large sample size of AAs to examine the association between obesity and prostate cancer aggressiveness by race individually and jointly.

Unlike the report of study of the SEARCH database, this study found that the association between obesity and aggressiveness seemed to be stronger among CAs. AAs have the highest incidence and mortality from prostate cancer in the world. This study could capture the elevated risk of developing high aggressive cancer

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among AAs compared with CAs even when comparing normal weight AAs to normal weight CAs. Because of elevated risk of developing aggressive prostate cancer in even normal weight AAs, the effect of obesity on prostate cancer aggressiveness may be partially masked when using normal weight AAs as the reference group. However, the picture was clearer when normal weight CAs were used as the reference group to evaluate the association between obesity and prostate cancer aggressiveness. Being obese or severely obese may increase the likelihood of having high aggressive prostate cancer beyond the effect of race alone.

To explain the different patterns observed between races, the first hypothesis was that the risk of developing high aggressive prostate cancer differed between races because CAs received more frequent care and screening. More frequent screening may lead to earlier detection. Therefore, the cancer was more likely to reflect a rapidly proliferating cancer in CAs when diagnosed with aggressive cancer. On the other hand, AAs presenting with aggressive disease were more likely to have a later diagnosis because they had more time to reach an aggressive state prior to diagnosis. To control for indicators that might capture differences in access to care, such as having had medical visits in the year prior to diagnosis, prostate cancer screening history was included as a covariate. CAs had been screened for PSA more often than AAs (71.0% vs. 45.6%). However, adjusting for screening history and screening frequency did not impact risk of developing aggressive prostate cancer related to obesity.

Another possible explanation of racial differences in prostate cancer aggressiveness is that prostate cancer was more difficult to detect among obese men, which delays diagnosis (8). Greater prostate volumes among obese men may modify the association between BMI or WHR and prostate cancer. Obesity-related prostate enlargement has been reported to obscure the association between BMI and prostate cancer (35). Obese men have lower likelihood of capturing prostate tissue upon needle biopsy, increased false-negative rate upon rectal examination, and lower PSA values than lean men (36). Biased treatment by race might explain the difference if less effort is made to conduct a thorough examination for prostate cancer in AAs, or if AAs who are obese are more obese than obese CAs. If the latter were true, and false-negative rates were related to the amount of adipose tissue present, the criteria, such as BMI and WHR, used would be too crude to detect such an effect. More sophisticated technology, such as dual-energy X-ray absorptiometry to quantify body fatness may be needed, which was beyond the scope of PCaP.

Inherent differences in stature by race have led to arguments that different BMI cutoffs should be used for different races (37). Other studies have reported that AA men on average were taller than other racial/ethnic group men, which raises the question of whether their higher BMI is less predictive than when BMI is used in populations of shorter men. A weak positive relationship between height and advanced, but not clinically localized, prostate cancer has been described in some populations (2, 9, 10, 38–40), although in most cases the relationship found was independent of obesity. However, height was not associated with aggressiveness among Africans or CAs in the PCaP study population.

Given that a racial difference remains after consideration of these factors, another hypothesis is that prostate cancer aggressiveness differs between AAs and CAs as a result of genetic variants or gene–environment interactions that differ by race. Specifically, racial differences in the type and prevalence of polymorphisms within genes or regulatory elements related to pathways involved in obesity and prostate cancer, such as testosterone and estrogen metabolism and IGF-I axis genes, may offer a partial explanation.

This study has certain limitations. First, prostate cancer aggressiveness was determined on the basis of the clinical characteristics of the disease at the time of diagnosis. Significantly higher proportion of CAs had higher education, higher household income, and received more frequent prostate cancer screening than AAs in PCaP. Consequently, the elevated PSA level, Gleason score, and clinical stage, which were used to determine cancer aggressiveness, might result from later diagnosis among AAs. PCaP has not yet collected information about biochemical progression-free, disease-free, or overall survival of the research subjects. Efforts to collect outcome information are underway in North Carolina and will start soon in Louisiana. Second, neither BMI derived from the self-reported body weight prior to cancer diagnosis nor the interviewer-measured weight after cancer diagnosis was perfect to assess the association between obesity and cancer aggressiveness. The former suffered from the inaccuracy of recalled body weight 12 months prior to cancer diagnosis, and the latter was prone to weight loss as the result of cancer or treatment. Therefore, the association between BMI from both measures and aggressiveness was presented. Although the magnitude of the association was less for the postcancer diagnosis BMI among CAs than the recalled weight BMI, and vice versa, for AAs, the pattern of the association was similar.

In conclusion, a positive association between BMI and prostate cancer aggressiveness with clear dose–response relationship was found. WHR greater than 0.98 was also associated with prostate cancer aggressiveness. AAs have more aggressive prostate cancer than normal BMI CAs, regardless of obesity status. Therefore, the association between high aggressive prostate cancer and extreme BMI in AAs, although present, was not as apparent as in CAs. These findings provide further support for the hypothesis that obese men tend to have more aggressive prostate cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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