Is Body Mass Index the Best Adiposity Measure for Prostate Cancer Risk? Results From a Veterans Affairs Biopsy Cohort

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OBJECTIVE To test multiple adiposity measures and prostate cancer (PC) risk in men undergoing prostate biopsy. We hypothesized that body mass index (BMI), body fat, and waist circumference would be highly correlated, and all would be associated with aggressive PC, but not overall risk.

SUBJECTS AND METHODS A case (483)-control (496) study among men undergoing prostate biopsy from 2007 to 2016 was conducted at the Durham Veterans Affairs Medical Center. Anthropometric and self-reported measurements were taken. Percent body fat was measured. Associations between adiposity measures and PC risk and high-grade PC (Gleason ≥7) were examined using logistic regression.

RESULTS BMI, percent body fat, and waist circumference were highly correlated ($\rho \geq .79$) ($P < .001$). On multivariable analysis, BMI ($P = .011$) was associated with overall PC risk, but percent body fat ($P = .16$) and waist circumference ($P = .19$) were not. However, all adiposity measurements were associated with high-grade disease ($P < .001$). We found a strong relationship between self-reported and measured weight ($\rho = .97$) and height ($\rho = .92$).

CONCLUSION BMI, body fat, and waist circumference were all highly correlated and associated with aggressive PC. This study supports the idea that higher adiposity is selectively associated with high-grade PC and reinforces the continued use of self-reported BMI as a measure of obesity in epidemiologic studies of PC. UROLOGY 105: 129–135, 2017. Published by Elsevier Inc.

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Prostate cancer (PC) and obesity are major public health problems. The association between these common entities has been subject to increased investigation in the last decade, and multiple epidemiologic studies have suggested that obesity is associated with increased risk and death from multiple types of cancer such as breast and colon cancer.[1-3] However, the relationship between obesity and PC risk is less clear.[4,5] Current evidence suggests that obesity, typically assessed by body mass index (BMI), is a risk factor for aggressive PC but is unrelated or even protective for overall PC.[6-8] BMI is widely used as a surrogate marker for obesity, as it is easy to measure, inexpensive, routinely collected in clinic settings, and is available in most patient medical records, or can be calculated using self-reported weight and height.[9]

However, it may not be an ideal surrogate, as BMI is influenced by both adipose and non-adipose tissue (ie, bone, muscle mass, etc).[10,11] Moreover, BMI does not take into consideration adipose distribution (central vs peripheral adiposity).[11] Finally, the degree to which self-reported body

weight correlates with actual weight is of concern and likely dependent on the lag time that a participant is required to recall. Collectively, these limitations might explain some of the inconsistent findings and obscure the association between obesity and PC. The use of bioelectric impedance analysis to estimate the percent of body fat and waist circumference to estimate central adiposity might provide a clearer picture of the association between adiposity and PC. Waist circumference is a measure of abdominal fat and is a simple technique that can be used to screen for obesity in men.[12,13] However, few PC research studies have evaluated the associations between BMI, waist circumference, body fat, and PC risk simultaneously in the same population to determine which is the best predictor.[14]

To evaluate the associations between multiple measures of adiposity and PC risk, we examined measured and self-reported data and took clinical measurements from men undergoing prostate biopsies at the Durham Veterans Affairs Medical Center (DVAMC) in North Carolina. We hypothesized that BMI, body fat, and waist circumference would be highly correlated with each other, and that all of them would be associated with aggressive PC, but not overall PC risk. In addition, we studied if self-reported height and weight strongly correlate with measured values, which would obviate the need to measure these in future epidemiologic studies of PC risk. If true, despite the limitations of BMI at an individual level, these results would support the use of self-reported BMI in epidemiologic studies of PC.

SUBJECTS AND METHODS

Study Design

Data were obtained from an ongoing case-control study of veterans undergoing prostate biopsy for concerns about PC at the DVAMC in Durham, North Carolina. The study was approved by the institutional review board at the DVAMC and written informed consent was obtained from all subjects before enrollment. Subjects were recruited between January 2007 and July 2016 from the urology clinic at the DVAMC. Eligible subjects were men with no prior history of PC who were undergoing a prostate needle biopsy because of abnormal prostate-specific antigen (PSA) or suspicious digital rectal examination (DRE) as clinically indicated. Biopsy was typically done for elevated PSA or rectal examination, although there was no set threshold to define elevated and was at the discretion of the treating physician. Of the 1714 eligible cases, 1116 consented to participate (65% response rate). We excluded 131 patients due to missing age, race, PSA, DRE, data on whether the subject had received any previous biopsy, prostate volume, percent body fat, waist circumference, or BMI. Of the 979 men who underwent a biopsy and were included in the analysis, 483 (49%) were biopsy-positive (cases) and 496 (51%) were biopsy-negative (controls).

Subjects were asked to self-report weight, height, and race. Age and history of prior biopsy were abstracted from the medical records. Measurements of weight and height were taken by trained personnel and used to calculate BMI (kg/m^2). Percent body fat was measured using bioelectrical impedance (Omron HBF-306 Fat Loss Monitor, Omron Healthcare, Inc., Hoofddorp, Netherlands). Prostate volume (in cubic centimeters) was estimated using transrectal ultrasound (TRUS) at the time of biopsy. Gleason score, obtained from the pathologic report of the biopsy, was categorized as low-grade (Gleason sum 2-6) or high-grade (Gleason sum 7-10) disease.

Statistical Analysis

We tested the association between biopsy outcome (cancer vs no cancer) and clinical variables using chi-square (χ^2) for categorical variables, *t* tests for normally distributed continuous variables, and rank-sum for non-normally distributed continuous variables. Similarly, we examined the association between cancer grade (low-grade: Gleason 2-6 vs high-grade: Gleason 7-10) and clinical variables. Variables included age (continuous), race (black vs non-black), PSA (logarithmically transformed, continuous), DRE findings (abnormal vs normal), TRUS prostate volume (logarithmically transformed, continuous), BMI (continuous), family history of PC (yes vs no vs unknown), percent body fat (continuous), waist circumference (continuous), and Gleason score (2-6, 7, and 8-10). The correlations between adiposity measures and both self-reported and measured body height and weight were tested using the Spearman correlation test. Similarly, Spearman correlation was used to test the correlation between adiposity measures and clinical characteristics.

We used logistic regression to assess risk of cancer vs no cancer. Because BMI, percent body fat, and waist circumference were highly correlated, we fit them in separate models to avoid collinearity. A Bland-Altman plot for self-reported vs actual weight was used to compare both measurement techniques. We also used multinomial logistic regression models to examine the relationships between the adiposity measures and risk of low-grade cancer (vs no cancer) and high-grade cancer (vs no cancer).

For all logistic and multinomial logistic regression models, we fit both unadjusted and adjusted models to account for confounders. In the multivariable model, we adjusted for age (continuous variable), race (black, white, other), previous biopsy (yes, no), family history of PC (yes, no), and factors that could predict the detectability of an existent tumor, including PSA (continuous logarithmically transformed), DRE findings (suspicious for cancer vs not), and TRUS prostate volume (continuous logarithmically transformed). A sensitivity analysis was performed to assess risk of high-grade PC with high-grade defined as Gleason ≥4 + 3. An α-level of 0.05 was set as the threshold for statistical significance for all analyses. All statistical analyses were performed using Stata 13.0 (StataCorp, College Station, TX).

RESULTS

Of the 979 men in our study cohort, 483 (49%) were diagnosed with PC from the biopsy. Patients who were diagnosed with PC were more likely to be black (64% vs 51%; $P = .001$), had higher median PSA (6.4 vs 5.5 ng/mL; $P < .001$), were more likely to have an abnormal DRE (28% vs 20%; $P = .007$), and had smaller median prostate volumes (34 cc vs 49 cc; $P < .001$), relative to biopsy-negative men (Table 1). There were no statistically significant differences between biopsy status and age, BMI, percent body fat, or waist circumference (all $P > .3$).

There were 237 (49%) patients diagnosed with high-grade PC and 237 (51%) with low-grade PC. Patients with high-grade PC had higher median PSA (7.4 vs 5.8 ng/mL; $P < .001$), relative to patients with low-grade PC, more often had abnormal DREs (39% vs 17%; $P < .001$), and had