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Original article

Anthropometric differences in obese men with biochemical failure after radical retropubic prostatectomy

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Abstract

Objective: The effect of obesity on biochemical failure after radical retropubic prostatectomy (RRP) is controversial. The differences in study outcomes may be a result of using body mass index (BMI) rather then direct anthropometric measurements of fat distribution. To investigate these differences, we used endorectal coil MRI (eMRI) data to directly measure fat thicknesses in obese men who underwent RRP.

Methods: We performed a retrospective analysis on an RRP database of 1,987 men with available BMI, clinicopathologic characteristics, and biochemical follow-up. Obese men (BMI $\geq$ 30) were compared with normal weight men (BMI $\leq$ 25) and overweight men (BMI $>$ 25, $<$ 30) for clinical and pathologic differences and biochemical failure. The eMRI data for 143 obese men were reviewed and the fat thicknesses in the anterior, posterior, and total anteroposterior abdominal diameters were measured and averaged in 3 separate images at and around the midline in the widest segment of the sagittal T2 weighted localizing scans.

Results: Kaplan Meyer curves with log rank analysis revealed a significant difference in biochemical free survival in lean men and overweight men compared with obese men ($P = 0.016$, $P = 0.021$). A BMI $\geq$ 30 did not predict time to biochemical failure on multivariate analysis (HR 1.02, 95% CI 0.67–1.56, $P = 0.29$). The anterior fat thickness on eMRI in obese men with biochemical failure ($n = 21$) was significantly smaller than obese men without biochemical failure ($n = 122$) (35 mm vs. 44 mm, $P = 0.003$). Calculated percent visceral fat thickness was also significantly larger in obese men with biochemical failure (74% vs.71%, $P = 0.02$). Subset analysis on patients with extracapsular extension and higher pathologic Gleason scores revealed similar trends in anterior and percent visceral fat thicknesses ($P = 0.003$, $P = 0.02$).

Conclusion: Difference in fat distribution may help account for some of the controversy surrounding obesity and prostate cancer. These differences may explain why BMI alone may not adequately predict the influence of obesity on outcomes of prostate cancer treatment.

Keywords: Prostate cancer; Obesity; Anthropometric; Radical retropubic prostatectomy; Biochemical failure; Visceral fat; superficial fat

1. Introduction

Obesity is a growing epidemic throughout the United States and has been linked with several types of cancers including colon, breast, thyroid, renal, and esophageal cancers [1]. The association between prostate cancer and obesity, however, is more controversial. Several studies have shown that an increased body mass index (BMI) is associated with increased risk of biochemical failure after radical retropubic prostatectomy (RRP), while other studies have found no association [2–6].

BMI is the most commonly used marker for obesity in the medical literature [7]. It is defined as weight in kilogram divided by height in meters squared. BMI, however, has several limitations. It does not properly classifying large, muscular individuals with little body fat, nor does it quantify the anthropometric differences associated with fat distributions, such as visceral vs. superficial fat. These limitations of BMI may be the source of conflicting data linking obesity and prostatic cancer.

Modern cross-sectional imaging affords opportunities to transcend the shortcomings of BMI and can be used in addition to other anthropometric measurement to classify fat

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distributions [8,9]. Endorectal coil magnetic resonance imaging, which is routinely performed in men with prostate cancer at our institution, also allows quantification and comparison of subcutaneous and visceral adipose content. In this study, we sought to evaluate whether characteristics of an individual's fat distribution predicted disease progression in men with localized prostate cancer.

2. Methods

After appropriate approval from the Institutional Review Board at the University of Pennsylvania, we identified and reviewed the available data on 1989 patients in our prospectively maintained prostate cancer database who underwent open RRP from 1991 to 2005. The data consisted of patient height, weight, race, age, clinical stage, grade of cancer at diagnosis, preoperative PSA values, and tumor characteristics at surgery (tumor grade, tumor volume, stage, and surgical margin status).

BMI, (weight in kilograms divided by height in meters squared) was assigned the National Institutes of Health classification of normal weight (<25 kg/m^2), overweight (≥ 25, <30 kg/m^2), obese (≥ 30 kg/m^2). Underweight patients with BMI < 18.5 ($n = 9$) were included in the normal weight classification and severely obese patients with BMI > 35 ($n = 51$) were included in the obese classification. Patients were monitored postoperatively with digital rectal examinations and serum PSA determinations every 3 months for 2 years, every 6 months for an additional 3 years, and yearly thereafter. Biochemical recurrence was defined as an increase in the serum PSA level > 0.2 ng/mL on 2 separate occasions.

eMRI was available for review in a total of 143 men with a BMI ≥ 30 . The T2 weighted sagittal localization images were used for analysis (Fig. 1). The umbilicus was identified as the midline section. Measurements of the largest anteroposterior (AP) diameter, anterior abdominal fat (measured as the fat thickness between the skin and anterior abdominal musculature), and posterior abdominal fat (measured as the fat thickness between the skin and posterior musculature) were then taken at the midline and at 1 cut immediately to the left and right of midline. These measurements were then averaged for the final measurement. All measurements were performed in a blinded manner by a single person (C.M.). The percent visceral fat was calculated as the anterior plus posterior abdominal wall fat thickness subtracted from the total AP diameter divided by the total AP diameter and expressed as a percentage.

2.1. Statistical analysis

Continuous variables were analyzed using an analysis of variance and χ^2 for categorical variables. PSA was examined using logarithmic transformation of (PSA + 1). Biochemical free survivorship was analyzed using the Kaplan-Meier method and time to recurrence was compared using a log-rank survivorship analysis. Univariate and multivariate Cox proportional hazard ratio models were used to estimate the relative risk of progression associated with obesity as a categorical and continuous variable. All statistical analyses were performed using STATA software, ver.9.0 (Stata Corp., College Station, TX).

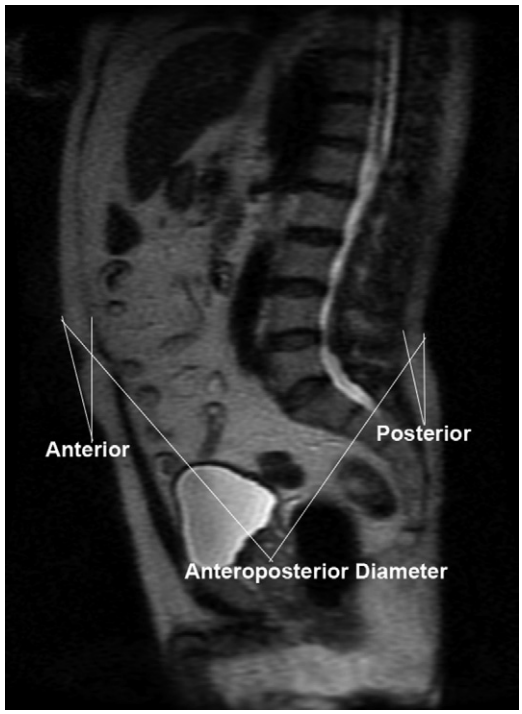

Fig. 1. Representation of the T2 weighted sagittal localization images obtained on endorectal coil MRI. The largest anterior, posterior, and total anteroposterior diameter were obtained in 3 images around the midline and the results were averaged.

3. Results

Over the past 14 years, the BMI in men undergoing RRP at our institution steadily increased (Spearman r = 0.1124, $P < 0.001$). The clinicopathologic characteristics of this entire study population separated by BMI classification are summarized in Table 1. A significantly greater proportion of African Americans were within the obese group compared with the normal weight and overweight group (14.76% vs. 8.89%, 9.9%, $P = 0.032$). Obese men also had a significantly greater proportion of positive surgical margins (24.5% vs. 18.34%, 15.42%, $P = 0.001$), extracapsular extension (66%, vs. 61.2%, 55.47%, $P = 0.004$), and were significantly younger than overweight and normal weight men (58.2 years vs. 59.8 years, 60.2 years, $P = 0.001$).

Biochemical progression-free survival was analyzed with Kaplan-Meier curves (Fig. 2). Log rank analysis revealed a significantly lower progression-free survival in obese men compared with overweight and normal weight