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Obesity, Risk of Biochemical Recurrence, and PSADT after Radical Prostatectomy: Results from the SEARCH Database

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Abstract

Objectives: To examine the association between body mass index (BMI) and aggressive biochemical recurrence (BCR) using the Shared Equal Access Regional Cancer Hospital (SEARCH) database.

Material and Methods: We identified 4,123 men with complete data treated by radical prostatectomy between 1988 and 2015. We tested the association between BMI and BCR using Cox models and among men with BCR, PSA doubling time (PSADT) was compared across BMI categories using linear regression. Models were adjusted for age, race, PSA, biopsy Gleason score, clinical stage, year, and surgical center.

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Results: Overall, 922 men (22%) were normal weight (BMI <25 kg/m2), 1863 (45%) were overweight (BMI 25–29.9), 968 (24%) were obese (BMI 30–34.9), and 370 (9%) were moderately or severely obese (BMI ≥35). After adjustment for multiple clinical characteristics, higher BMI was significantly associated with higher risk of BCR (p=0.008). Among men with a BCR, men in the four BMI categories had similar multivariable adjusted PSADT values (increasing BMI categories: 20.9 vs. 21.3 vs. 21.0 vs. 14.9 months, p=0.48).

Conclusion: While we confirmed higher BMI was associated with BCR, we found no link between BMI and PSADT at the time of recurrence. Our data suggest obese men do not have more aggressive recurrences. Future studies are needed to test whether obesity predicts response to salvage therapies.

Keywords

Prostate cancer; radical prostatectomy; obesity; PSA recurrence; PSADT

INTRODUCTION

More than one in three adults in the United States is obese [1]. As a result, there is an increasing awareness of the medical problems related to obesity including heart disease, diabetes, hypertension, and cancer. In terms of prostate cancer, obesity is associated with 20–30% increased risk of prostate cancer death [2]. Though on a percentage basis, this association may be modest, the high prevalence of prostate cancer translates into thousands of excess deaths from obesity-related prostate cancer.

There are many possible reasons obese men may be at increased risk of PCSM. For example, there may be difficulties in detecting prostate cancer in obese men (lower PSA values [3] and larger sized prostates [4]), which could delay diagnosis. Alternatively, once diagnosed, treatment may not be as efficacious in obese men. Indeed, a prior study of men undergoing radical retropubic prostatectomy by experienced high-volume surgeons found the rate of capsular incision (i.e. cutting into the prostate and a sign of a less-than-ideal operation) was higher for obese men [5]. Similarly, most surgical series found higher rates of positive margins among obese men [6–8]. Even after adjusting for excess positive margins, a meta-analysis found obese men were at increased risk of biochemical recurrence (BCR) risk after surgery [9].

More recently, we showed obesity is more strongly linked with increased risk of prostate-cancer specific mortality (PCSM) after radical prostatectomy than BCR, albeit based on a small number of deaths [10]. While it has been shown that overall survival in men with BCR after radical prostatectomy is comparable to men without a detectable PSA after surgery [11], it is less clear why obesity is more strongly linked with PCSM. The fact that the link between obesity and PCSM was stronger than with recurrence suggests that either recurrences are more aggressive or that obesity predicts poorer responses to salvage therapies such as hormonal therapy. We hypothesized that more aggressive recurrences explain the stronger link between obese men and PCSM after radical prostatectomy than with recurrence. To test this hypothesis, we examined the association between body mass index (BMI) and aggressive BCR, using PSA doubling time (PSADT) as a measure of

disease aggressiveness, given PSADT has been shown to correlate with PCSM [12]. To accomplish this, we used the multi-center, multi-ethnic Shared Equal Access Regional Cancer Hospital (SEARCH) Database [13].

MATERIALS AND METHODS

Study design

After obtaining approval from the Institutional Review Board, data from men undergoing radical prostatectomy from 1988 to 2015 at six Veterans Affairs hospitals (Palo Alto, West Los Angeles, and San Diego, CA; Durham and Asheville, NC; Augusta, GA) were retrospectively collected in the SEARCH database. Patients who received neoadjuvant androgen deprivation or radiation therapy were not included in the database. Information was collected on demographic, clinical, and pathological factors and patients were followed up through 2016. From a total cohort of 5,513 men, we excluded men missing race (n=26), PSA (n=168), clinical stage (n=440), biopsy (n=324) or pathological (n=35) grade group, BMI (n=177), pathological features (n=143), or follow-up (n=76), resulting in a final study cohort of 4,123 men.

We stratified men into four groups based on BMI: normal weight (BMI <25 kg/m^2), overweight (BMI 25–29.9 kg/m^2), mildly obese (BMI 30–34.9 kg/m^2), and moderately or severely obese (BMI ≥35 kg/m^2). BCR was defined as a single PSA >0.2 ng/ml, two concentrations at 0.2 ng/ml, or secondary treatment for an elevated postoperative PSA. Men were followed through the VA system and all PSA data were abstracted. Clinic notes were reviewed to collect outside PSA data. Among all patients, the median (interquartile range (IQR)) number of post-operative PSA tests was 14 (9, 21).

Statistical analysis

PSADT was calculated by log(2) divided by the slope of the linear regression of log(PSA) over time in months. Subjects with PSADT <0 or >120 were assigned 120 months for ease of analysis. All PSA values two years after the date of recurrence but before secondary treatment were used to calculate PSADT. This calculation required at least two PSA values over at least three months.

Characteristics were compared among BMI groups using Kruskal-Wallis tests for continuous variables and chi-squared tests for categorical variables. The association between BMI and time to BCR was tested using Cox proportional hazards models, adjusted for age (continuous), race (black vs. white. vs. other), grade group (1–5), clinical stage (T1 vs. T2-T4), pre-operative PSA (continuous), year of surgery (continuous), and surgical center. BMI was treated as a continuous and categorical variable. For the categorical analysis, a p-trend was calculated by assigning the median BMI of each category to patients in that category and treating this variable as a continuous variable in the model.

To test whether obese men had shorter PSADT at the time of recurrence, we fit a linear regression model with log-transformed PSADT as the outcome and categorical BMI as the main predictor. We then used predictions from the model to estimate the mean-multivariable adjusted PSADT and standard deviation for each BMI group. The estimates were

exponentiated to be interpreted in months. In the first model, we adjusted for demographic and clinical characteristics, including age (continuous), race (black vs. white. vs. other), biopsy grade group (1–5), clinical stage (T1, T2-T4), pre-operative PSA (continuous), year of surgery (continuous), and surgical center. In the second model, we adjusted for demographic and pathological characteristics, including age (continuous), race (black, white, other), pathological grade group (1–5), positive surgical margins, extracapsular extension, seminal vesicle invasion, positive lymph nodes, pre-operative PSA (continuous), year of surgery (continuous), and surgical center. This analysis was repeated, stratifying by race (black/non-black) and age (<60, 60–64, ≥65).

Finally, we investigated whether obese men were more likely to have an incalculable PSADT and thus biased our results given an incalculable PSADT may be a sign of more aggressive disease [14]. We used a logistic regression model with calculable PSADT (yes vs. no) as the outcome and BMI (continuous) as the main predictor. This model was adjusted for demographic and disease characteristics as described above.

All statistical analyses were performed using STATA 13.0 (Stata Corp., College Station, Texas).

RESULTS

Patient Characteristics

Overall, 922 men (22%) were normal weight, 1863 (45%) were overweight, 968 (24%) were obese, and 370 (9%) were moderately or severely obese (Table 1). Higher BMI group was associated with younger age at surgery ($p<0.001$), more recent year of surgery ($p<0.001$), lower PSA ($p<0.001$), higher grade group ($p=0.001$), and larger prostate weight ($p<0.001$). There was no association between BMI group and race, clinical stage, pathological grade group, positive surgical margins, extracapsular extension, seminal vesicle invasion, positive lymph nodes, or follow-up time (all $p>0.05$).

BMI and BCR

Median follow-up was 89 months (interquartile range: 51–138) and 1382 (34%) men had a BCR. On multivariable analysis, higher BMI was associated with increased risk of BCR (HR 1.02, 95% CI 1.00–1.03, $p=0.008$). After categorizing BMI into 4 groups, men who were mildly obese had higher risk of BCR (HR 1.19, 95% CI 1.02–1.39), but the trend between higher BMI group and risk of BCR was not statistically significant ($p=0.076$). (Table 2)

BMI and PSADT

The median (IQR) number of PSA values used to calculate PSADT was 4 (3–6), and this was similar across BMI groups ($p=0.23$). Of the 1,382 men who had a BCR, 330 (24%) recurred due to early salvage treatment and thus do not have a PSADT calculable. Of the remaining 1,052 (76%) men who recurred due to a rising PSA, PSADT was calculable for 652 patients. After adjusting for demographic and clinical characteristics, men in the four BMI categories had similar multivariable-adjusted PSADT values (increasing BMI categories: 20.9 vs. 21.3 vs. 21.0 vs. 14.9 months, $p=0.27$). Results were similar after

adjusting for pathological characteristics (p=0.48; Table 3). When stratified by race or age, similar results were seen in that PSADT was similar across age groups and races (Supplementary Table 1).

BMI and calculable PSADT

To explore whether obese patients were more likely to have incalculable PSADT which we have previously shown corresponds with worse disease [14], we tested whether BMI was associated with incalculable PSADT. After adjusting for demographic and disease characteristics, we found obesity was not independently associated with missing PSADT (p=0.36). In other words, obese patients were no more likely to have non-calculable PSADT (Table 4).

DISCUSSION

Obesity is associated with 20–30% increased risk of PCSM [2]. Determining which exact steps within the path from cancer development, to progression, to resistance to treatments to PCSM that are influenced by obesity may provide novel insights into how obesity influences prostate cancer biology. We previously showed that obesity is associated with increased risk of BCR after radical prostatectomy, however obesity was more strongly associated with PCSM, suggesting events after recurrence or the aggressiveness of the recurrence may influence long-term outcomes [10]. Toward that end, herein we examined the association between obesity and tumor aggressiveness at the time of recurrence after surgery. Similar to our prior findings [6] and in-line with a meta-analysis [9], we found higher BMI was linked with greater recurrence risk. However, we found no association between BMI and aggressive recurrence, as measured by PSADT. This suggests later events such as response to subsequent therapies (i.e. hormonal therapy) may explain the stronger link between obesity and PCSM than that seen between obesity and BCR after surgery.

Multiple studies examined the association between obesity and outcomes after radical prostatectomy. Though individual studies have varied, a meta-analysis found each 5kg/m^2 increase in BMI increased BCR rates after radical prostatectomy by 18% in studies from the US [15]. Consistent with this, we found higher BMI was associated with increased BCR risk. As such, there is little doubt that higher BMI is linked with greater BCR. However, whether BMI influences the aggressiveness of the recurrences and later events (i.e. response to salvage therapies) is less well-studied.

To investigate whether obese men have more aggressive recurrences, we examined the association between BMI and PSADT at BCR given that among men treated with radical prostatectomy, PSADT at the time of BCR after radical prostatectomy is a strong predictor of disease progression and PCSM [12]. We found no association between BMI and PSADT at the time of BCR. Thus, while obese men were more likely to recur, the idea that the recurrences were more aggressive does not explain why obese men are much more likely to have PCSM as seen in this cohort in a prior study [10].

If confirmed in future studies, there are several possible explanations for the stronger relationship between BMI and PCSM. For one, given that higher BMI is not linked to more

aggressive recurrences, obesity must be associated with a poorer response to salvage treatments. In particular, responses to androgen deprivation therapy may be worse. First off, obese men have lower testosterone levels and therefore tumors in obese men may be partially androgen resistant (i.e. they developed and grew in a lower-androgen environment). Consistent with this, multiple studies show tumors diagnosed in men with lower testosterone are more aggressive [16, 17]. Second, given that the same dose of luteinizing hormone releasing hormone (LHRH) analog is given regardless of BMI (i.e. unlike various chemotherapies which are dose per body surface area, doses for LHRH are fixed), this may lead to under-dosing in obese men. In-line with this possibility, data suggest that testosterone levels on hormonal therapy are higher in obese men [18]. As higher nadir testosterone levels are linked with increased risk of developing castration-resistant disease [19], higher nadirs in obese men may contribute to poorer response to hormonal therapy. Collectively, these factors all suggest obese men may not respond as well to hormonal therapy. Indeed, we previously found higher BMI at the time of androgen deprivation therapy is associated with greater risk of developing metastases and castrate-resistant disease [20], though those results were based upon small numbers. Thus, further studies are needed to better confirm the possible association between obesity and poor response to hormonal therapy. An alternative, and purely speculative explanation for the stronger link between obesity and PCSM than BCR, is that the greater metabolic milieu of obesity that leads to increased prostate cancer aggressiveness at diagnosis [10], may lead to continued evolutionary pressure and increased tumor aggressiveness over time. Ultimately, future studies are needed to better understand the link between obesity and PCSM.

In the current study we used PSADT as a measure of disease aggressiveness. While not all men who develop a BCR will die from prostate cancer [12], PSADT is one of the strongest predictors of PCSM.[12, 21] Given this strong association, it is worth noting recent literature showed due to secondary therapy often given for high risk recurrences and the fact that many patients will have secondary treatment before having enough PSA values to calculate PSADT, those with a calculable PSADT could represent a lower risk cohort [14]. Indeed, in the current study, about 24% of patients recurred due to early salvage treatment and thus did not have a calculable PSADT. Additionally, of those who recurred due to a rising PSA, about 38% did not have a PSADT calculable. However, we found obesity was unrelated to having a non-calculable PSADT. Thus, while PSADT data were missing on a number of patients, this was unrelated to BMI and thus likely had no effect on our overall conclusions.

Though the number of patients was reasonable (n=652 with PSADT data), further studies with even larger cohorts are needed to confirm our findings. This is particularly true for men in the highest BMI group who had an estimated 6 month shorter PSADT. However, the previously noted stronger link between obesity and PCSM vs. a weaker link with recurrence was seen even in overweight men for which we found no evidence of differences in PSADT. [10] Thus, while larger studies are needed, they are unlikely to significantly change our conclusions. PSA was not measured in a systematic fashion leading to perhaps less accurate assessments of true PSADT. While PSA measurements are likely non-differential by BMI, future studies should use an optimized systematic fashion to measure PSA regularly. As noted, PSADT was missing on a large percent of patients, though BMI was unrelated to the likelihood of missing PSADT. Also, grade group was measured over many years and there

have been changes over time in prostate cancer grading. We adjusted for year of surgery to account for these changes and thus how this affects our results is not clear. Finally, our measurement of disease aggressiveness was PSADT. Though PSADT is well-validated as associated with aggressive disease, other measures such as time to metastases in the absence of hormonal therapy would better capture tumor growth without secondary therapies. However, such an analysis may be difficult given most men receive hormonal therapy prior to metastases today.

In a multicenter series of men undergoing radical prostatectomy, we found men with higher BMI were more likely to have BCR. However, we also found no link between BMI and PSADT at the time of recurrence. Given the known stronger association between obesity and increased PCSM after radical prostatectomy versus recurrence in general [10], our data suggest that the strength of the association with PCSM may not be due to more aggressive recurrences among obese men. Future studies are needed to study the effect of obesity and response to salvage therapies such as hormonal therapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

[1]. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. JAMA : the journal of the American Medical Association. 2016 6 7: 315:2284–91 [PubMed: 27272580]

[2]. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. The New England journal of medicine. 2003 4 24: 348:1625–38 [PubMed: 12711737]

[3]. Baillargeon J, Pollock BH, Kristal AR, et al. The association of body mass index and prostate-specific antigen in a population-based study. Cancer. 2005 1 24: 103:1092–5 [PubMed: 15668913]

[4]. Freedland SJ, Platz EA, Presti JC, et al. Obesity, serum prostate specific antigen and prostate size: implications for prostate cancer detection. The Journal of urology. 2006 2: 175:500–4 [PubMed: 16406980]

[5]. Freedland SJ, Grubb KA, Yiu SK, et al. Obesity and capsular incision at the time of open retropubic radical prostatectomy. The Journal of urology. 2005 11: 174:1798–801 [PubMed: 16217290]

[6]. Freedland SJ, Aronson WJ, Kane CJ, et al. Impact of obesity on biochemical control after radical prostatectomy for clinically localized prostate cancer: a report by the Shared Equal Access Regional Cancer Hospital database study group. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2004 2 1: 22:446–53 [PubMed: 14691122]

[7]. Amling CL, Riffenburgh RH, Sun L, et al. Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2004 2 1: 22:439–45 [PubMed: 14691120]

[8]. Siddiqui SA, Inman BA, Sengupta S, et al. Obesity and survival after radical prostatectomy: A 10-year prospective cohort study. Cancer. 2006 8 1: 107:521–9 [PubMed: 16773619]

[9]. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011 4: 4:486–501 [PubMed: 21233290]

[10]. Vidal AC, Howard LE, Sun SX, et al. Obesity and prostate cancer-specific mortality after radical prostatectomy: results from the Shared Equal Access Regional Cancer Hospital (SEARCH) database. Prostate cancer and prostatic diseases. 2017 3: 20:72–8 [PubMed: 27698439]

[11]. Jhaveri FM, Zippe CD, Klein EA, Kupelian PA. Biochemical failure does not predict overall survival after radical prostatectomy for localized prostate cancer: 10-year results. Urology. 1999 11//: 54:884–90 [PubMed: 10565752]

[12]. Freedland SJ, Humphreys EB, Mangold LA, et al. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. JAMA : the journal of the American Medical Association. 2005 7 27: 294:433–9 [PubMed: 16046649]

[13]. Wadhwa H, Terris MK, Aronson WJ, et al. Long-term oncological outcomes of apical positive surgical margins at radical prostatectomy in the Shared Equal Access Regional Cancer Hospital cohort. Prostate cancer and prostatic diseases. 2016 12: 19:423–8 [PubMed: 27698440]

[14]. Hamilton RJ, Aronson WJ, Terris MK, et al. Limitations of prostate specific antigen doubling time following biochemical recurrence after radical prostatectomy: results from the SEARCH database. The Journal of urology. 2008 5: 179:1785–9; discussion 9–90 [PubMed: 18343434]

[15]. Hu MB, Xu H, Bai PD, Jiang HW, Ding Q. Obesity has multifaceted impact on biochemical recurrence of prostate cancer: a dose-response meta-analysis of 36,927 patients. Med Oncol. 2014 2: 31:829 [PubMed: 24390417]

[16]. Massengill JC, Sun L, Moul JW, et al. Pretreatment total testosterone level predicts pathological stage in patients with localized prostate cancer treated with radical prostatectomy. The Journal of urology. 2003 5: 169:1670–5 [PubMed: 12686805]

[17]. Garcia-Cruz E, Piqueras M, Huguet J, et al. Low testosterone levels are related to poor prognosis factors in men with prostate cancer prior to treatment. BJU international. 2012 12: 110:E541–6 [PubMed: 22584031]

[18]. Smith MR. Obesity and sex steroids during gonadotropin-releasing hormone agonist treatment for prostate cancer. Clin Cancer Res. 2007 1 1: 13:241–5 [PubMed: 17200361]

[19]. Klotz L, O'Callaghan C, Ding K, et al. Nadir testosterone within first year of androgen-deprivation therapy (ADT) predicts for time to castration-resistant progression: a secondary analysis of the PR-7 trial of intermittent versus continuous ADT. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2015 4 1: 33:1151–6 [PubMed: 25732157]

[20]. Keto CJ, Aronson WJ, Terris MK, et al. Obesity is associated with castration-resistant disease and metastasis in men treated with androgen deprivation therapy after radical prostatectomy: results from the SEARCH database. BJU international. 2012 8: 110:492–8 [PubMed: 22094083]

[21]. D'Amico AV, Moul JW, Carroll PR, Sun L, Lubeck D, Chen MH. Surrogate end point for prostate cancer-specific mortality after radical prostatectomy or radiation therapy. Journal of the National Cancer Institute. 2003 9 17: 95:1376–83 [PubMed: 13130113]

Table 1.

Characteristics of cohort by BMI group

	Normal Weight (<25kg/m^2) (N=922)	Overweight (25-29.9kg/m^2) (N=1863)	Mildly obese (30-34.9kg/m^2) (N=968)	Moderately to Severely Obese (>=35 kg/m^2) (N=370)	p value
Age					<0.001[1]
Median	63	62	62	60	
Q1, Q3	59, 67	58, 66	58, 66	56, 64	
Year of surgery					<0.001[1]
Median	2005	2007	2008	2008	
Q1, Q3	2001, 2010	2002, 2011	2003, 2012	2004, 2011	
Race					0.079[2]
White	523 (57%)	1141 (61%)	558 (58%)	208 (56%)	
Black	371 (40%)	661 (35%)	380 (39%)	155 (42%)	
Other	28 (3%)	61 (3%)	30 (3%)	7 (2%)	
PSA (ng/mL)					<0.001[1]
Median	7.0	6.2	6.1	5.9	
Q1, Q3	5.0, 11.0	4.7, 9.4	4.7, 8.9	4.6, 9.2	
Grade group					0.001[2]
1	480 (52%)	839 (45%)	435 (45%)	143 (39%)	
2	239 (26%)	499 (27%)	275 (28%)	120 (32%)	
3	90 (10%)	260 (14%)	125 (13%)	48 (13%)	
4	91 (10%)	190 (10%)	90 (9%)	43 (12%)	
5	22 (2%)	75 (4%)	43 (4%)	16 (4%)	
Clinical stage					0.199[2]
T1	541 (59%)	1139 (61%)	610 (63%)	235 (64%)	
T2-T4	381 (41%)	724 (39%)	358 (37%)	135 (36%)	
Prostate weight (g)					<0.001[1]
Median	38.0	41.0	43.0	44.0	
Q1, Q3	30.0, 48.0	33.0, 52.2	33.0, 56.3	34.3, 54.8	
Pathological grade group					0.062[2]
1	304 (33%)	575 (31%)	274 (28%)	88 (24%)	
2	362 (39%)	692 (37%)	405 (42%)	159 (43%)	
3	151 (16%)	328 (18%)	169 (17%)	70 (19%)	
4	58 (6%)	148 (8%)	66 (7%)	31 (8%)	
5	47 (5%)	120 (6%)	54 (6%)	22 (6%)	
Positive surgical margins	355 (39%)	723 (39%)	407 (42%)	158 (43%)	0.192[2]
Extracapsular extension	169 (18%)	369 (20%)	166 (17%)	78 (21%)	0.235[2]
Seminal vesicle invasion	81 (9%)	181 (10%)	89 (9%)	43 (12%)	0.447[2]

	Normal Weight (<25kg/m^2) (N=922)	Overweight (25-29.9kg/m^2) (N=1863)	Mildly obese (30-34.9kg/m^2) (N=968)	Moderately to Severely Obese (>=35 kg/m^2) (N=370)	p value
Lymph node involvement					0.144[2]
no	596 (65%)	1208 (65%)	607 (63%)	217 (59%)	
yes	16 (2%)	39 (2%)	17 (2%)	13 (4%)	
not done	310 (34%)	616 (33%)	344 (36%)	140 (38%)	
Follow-up*					0.104[1]
Median	91.2	91.3	84.4	85.3	
Q1, Q3	50.6, 143.5	52.2, 140.7	48.2, 135.5	49.3, 132.8	

[1] Kruskal Wallis

[2] Chi-Square

'PSA=prostate-specific antigen, Q1=25th percentile, Q3=75th percentile, BMI=body mass index'

* Reported among patients who did not die during follow-up

Table 2.

Hazard ratios and 95% CI for biochemical recurrence after radical prostatectomy by body mass index

	Recurrence/ Total	Person-years	HR (95% CI)*	p-value
Biochemical recurrence				
Categorical				0.076≠
Normal weight	309/922	4755	Ref.	
Overweight	622/1863	10063	1.03 (0.90-1.18)	
Mild obesity	338/968	4703	1.19 (1.02-1.39)	
Moderate/severe obesity	113/370	1762	1.08 (0.87-1.35)	
BMI continuous	1382/4123	21273	1.02 (1.00-1.03)	0.008

*Adjusted for age, race, biopsy Gleason score, clinical stage, pre-operative PSA, year of surgery, and center

≠p-trend determined using median BMI of each category as a continuous variable

Table 3.

Mean multivariable adjusted PSADT (months) after radical prostatectomy by body mass index (N=652)

		PSADT ± SD	
	N	Model 1†	Model 2*
BMI			
Normal weight	922	20.9 ± 1.1	20.5 ± 1.1
Overweight	1863	21.3 ± 1.1	21.1 ± 1.1
Mild obesity	968	21.0 ± 1.1	21.3 ± 1.1
Moderate/severe obesity	370	14.9 ± 1.2	15.7 ± 1.2
P-value		0.27	0.48

† Adjusted for age, race, pre-operative PSA, biopsy Gleason score, clinical stage, year of surgery, and center

* Adjusted for age, race, pre-operative PSA, pathological Gleason score, positive surgical margins, extracapsular extension, seminal vesicle invasion, positive lymph nodes, year of surgery, and center

Table 4.

Association between BMI and having an incalculable PSA doubling time among patients who recurred

	OR (95% CI)*	p-value
Biochemical recurrence		
Categorical		0.36
Normal weight	Ref.	
Overweight	1.24 (0.61-1.04)	
Mild obesity	1.08 (0.76-1.52)	
Moderate/severe obesity	1.42 (0.87-2.31)	
BMI continuous	1.02 (0.99-1.04)	0.17

*Adjusted for age, race, pre-operative PSA, biopsy Gleason score, year of surgery, center, and time from surgery to recurrence