Published in final edited form as:
Obes Res Clin Pract. 2014 ; 8(4): e374–e381. doi:10.1016/j.orcp.2013.06.002.

Association of Body Mass Index and Prostate Cancer Mortality

Reina Haque, PhD[1], **Stephen K. Van Den Eeden, PhD**[2], **Lauren Wallner, PhD**[1], **Kathryn Richert-Boe, MD**[2], **Bhaskar Kallakury, MD**[3], **Renyi Wang, PhD**[1], and **Sheila Weinmann, PhD**[4]

[1]Research & Evaluation, Kaiser Permanente Southern California, Pasadena, CA

[2]Division of Research, Kaiser Permanente Northern California, Oakland, CA

[3]Georgetown University, Dept. of Pathology, Washington, DC

[4]Center for Health Research, Kaiser Permanente Northwest, Portland, OR

Abstract

Objectives—Inconsistent evidence exists on whether obesity is associated with an increased risk of prostate cancer death post-radical prostatectomy. We examined data from three large health plans to evaluate if an increased body mass index (BMI) at prostate cancer diagnosis is related to prostate cancer mortality.

Subjects & Methods—This population-based case-control study included 751 men with prostate cancer who underwent radical prostatectomy. Cases were men who died due to prostate cancer (N=323) and matched controls (N=428). We used multivariable logistic regression models to assess the association between BMI at diagnosis and prostate cancer mortality, adjusted for Gleason score, PSA, tumor characteristics, and matching factors.

Results—Study subjects were classified into the following BMI (kg/m^2) categories: healthy (18.5–24.9), overweight (25–29.9) and obese (≥ 30). Nearly 43% of the participants had a BMI ≥25 at diagnosis. A higher fraction of cases (30%) were obese compared to controls (22%). Overall, obese men had more than a 50% increase in prostate cancer mortality (adjusted odds ratio=1.50 [95% CI, 1.03–2.19]) when compared to men with healthy BMI. After stratifying by Gleason score, the odds of mortality generally rose with increasing BMI. The strongest effect was observed in the Gleason Score 8+ category (2.37, 95% CI: 1.11–5.09). These associations persisted after adjusting for PSA at diagnosis and other tumor characteristics.

Conclusions—These results suggest that BMI at diagnosis is strongly correlated with prostate cancer mortality, and that men with aggressive disease have a markedly greater odds of death if they are overweight or obese.

Corresponding and Reprints Author: Reina Haque, Ph.D., M.P.H., Kaiser Permanente Southern California, Department of Research & Evaluation, 100 South Los Robles Avenue, 2nd Floor, Pasadena, CA 91101, Phone: 011 (626) 564-5707, Fax: 011 (626) 564-3430, Reina.Haque@kp.org.

Keywords

BMI; prostate cancer; survival; population sciences; case-control

INTRODUCTION

Nearly 240,890 men were newly diagnosed with prostate cancer in 2011, and roughly 33,700 died due to the disease [1]. Known risk factors for prostate cancer incidence include age, African-American race/ethnicity, lower socio-economic status, family history of any cancer, and high body mass index [1–2]. However, after the initial prostate cancer diagnosis, it is unclear which individuals are at greater risk of mortality and if lifestyle factors (such as body weight) can impact survival. The biologic mechanism for obesity potentially affecting prostate cancer prognosis is not established, but prior studies have hypothesized that obesity is associated with higher grade tumors, disease progression, higher prostate specific antigen (PSA) levels after diagnosis [3–5], or lower testosterone levels, all of which can contribute to adverse prostate cancer outcomes [6]. Further, obtaining clear surgical margins is also difficult in obese patients who undergo prostatectomy [5].

Recent studies suggest that obesity around the time of prostate cancer diagnosis may affect survival, but many were limited by short follow-up time, or the timing for capturing of body mass index (BMI) data was not clear [7–10]. Obesity was associated with an increased risk of prostate cancer death in a pooled analysis of 424,519 participants in the Asia-Pacific Cohort Studies Collaboration (APCSC). In that analysis, excess weight increased the risk of prostate cancer mortality by 45% in obese men (HR=1.45 [95% CI: 0.97–2.19]) and by 41% in overweight men (HR=1.41 [1.14–1.74]) [9]. However, in the pooled APCSC analysis, it was unclear when BMI was captured in each of the individual studies. Rodriguez and colleagues also examined two large cohorts of adult men in the U.S. and similarly determined that BMI was associated with prostate cancer-specific mortality in both cohorts (RR=1.27, 1.04–1.56 in first cohort and RR=1.21, 1.07–1.37 in the 2nd) [11]. However, BMI was obtained before diagnosis and based on self-reported height and weight in that study. A few other studies examined how BMI affects biochemical recurrence based on prostate specific antigen (PSA); however, biochemical recurrence is not strongly correlated with mortality [12,13]. In addition, other studies were based on small number of deaths or lacked information on important covariates such as tumor characteristics [14]. Given the limitations and results of these prior studies, the objective of this study was to determine if BMI at prostate cancer diagnosis was related to prostate cancer mortality using height, weight and comorbidity data captured from medical records of men diagnosed and treated with prostatectomy in three large health maintenance organizations. Our hypothesis was that BMI at diagnosis was related to prostate cancer survival with obese and overweight men more likely to die due to their disease after accounting for comorbidities and other patient and clinical factors.

METHODS

Study design, setting and patients

The study population included men who were members of three large managed care organizations in California, and northwest Oregon and southwest Washington (Kaiser Permanente), diagnosed with prostate cancer from 1971– 2001 and treated with radical prostatectomy, and were either Non-Hispanic Whites or African-American, ≤ age 80 years, and health plan members for at least 12 months following their diagnosis. Potential subjects were identified through the SEER-affiliated (California) and health plan (Oregon/ Washington) cancer registries. The cause of death was ascertained through electronic linkage with each state's death certificate files (California) or cancer registry follow-up (Oregon/Washington) and confirmed with chart reviews conducted by the study oncologist (KRB).

We conducted a case-control study whereby cases were prostate cancer patients who subsequently died as a result of the disease and controls were prostate cancer patients who were alive at the time of the matched cases' death. Controls were individually matched on the following factors: 1) race, 2) age at diagnosis, 3) stage at diagnosis (American Joint Commission on Cancer TNM classification), 4) year of diagnosis, 5) health plan site, 6) duration of health plan membership before diagnosis and 7) at least as long duration of health plan membership after diagnosis. Among white participants, we matched 1 control per case, and among African-Americans the proposed ratio was 1:2 (however, for some AA cases, we only found one match). The study included 323 cases and 428 controls. The Institutional Review Boards from each of the three study sites reviewed and approved this study

Data elements

Information on the exposure and covariates were abstracted from standardized chart reviews by trained chart abstractors, and the SEER affiliated cancer registries. The exposure variable of interest was BMI (kg/m^2) at prostate cancer diagnosis. Because BMI was not always noted in the medical charts at the time of diagnosis, we captured height and weight six months pre or post-diagnosis. BMI was classified into three categories: healthy (18.5–24.9); overweight (25.0–29.9); and obese (≥30) [15,16]. Covariates included years of membership in the health plan, symptoms at diagnosis (e.g., urinary voiding; musculoskeletal pain; sexual dysfunction; abdominal pain), history of hypertension, diabetes and tobacco use before diagnosis, and prostate cancer recurrence. We also extracted information on prostate specific antigen (PSA) level at diagnosis, primary cancer treatment (mainly radiotherapy) and any adjuvant hormonal or neo-adjuvant treatment. Pathologic variables were assessed by an expert prostate cancer pathologist (BK). These variables included tumor grade, positive surgical margins, and lymph node status (positive or negative), and Gleason score. Gleason score was based on review of diagnostic pathology slides from the radical prostatectomy. Gleason score was categorized into three categories: <7; 7 (either 3+4 or 4+3 pattern); and ≥8.

Statistical Analysis

We initially examined proportions of BMI categories and covariates by case-control status. Distributions of these variables were compared using chi-square tests. In multivariable analyses, we performed conditional and unconditional logistic regression analyses to estimate crude and adjusted odds ratios (ORs), and 95% confidence intervals (CIs). Because the results were similar from the two models, we presented the unconditional results to enhance precision and power [17–19]. In addition to the potential confounding factors accounted for by matching (health plan site, race, age at diagnosis, year of diagnosis and stage at diagnosis, duration of health plan membership), we also included the following variables in unconditional logistic regression models: tumor grade, lymph node status, PSA at diagnosis, adjuvant radiotherapy, and surgical margins. Only those factors deemed to be significant in the descriptive analyses were ultimately included in the multivariate model. Because Gleason score is an important predictor for aggressive disease and may be related to BMI, we conducted separate analyses stratified by Gleason score. In all models, a two-sided test with an alpha level of 0.05 was used, and the healthy BMI group (BMI<25) was used as the reference group. All analyses were conducted using SAS version 9.2.

RESULTS

The final study group included 323 cases and 428 controls for a total of 751 men. The cases included 277 Caucasian and 46 non-Caucasians. The controls included 331 Caucasians and 97 non-Caucasians. Table 1 displays the demographic and clinical characteristics of the case and control groups. Of the 323 fatal cases, the majority of cases (n=266, 82%) were initially diagnosed with early stage disease (TNM stage II-III). (Note, among the men with stage IV disease who underwent radical prostatectomy, all had localized lymph node only disease). The majority of cases and controls were enrolled in the health plan for more than five years, with controls having longer membership duration (P<0.05). As expected, the distribution of age and year at diagnosis (matching factors) were similar in both groups. Also, as expected, higher percentage of fatal cases were symptomatic at diagnosis (i.e., had urinary voiding problems, musculoskeletal or abdominal pain, sexual dysfunction) versus controls (P=0.001). Among the cases initially diagnosed with TNM IV disease (18% of the cases), the prevalence of such symptoms was greater in such cases than in cases initially diagnosed with TNM II-III (P<0.05). The majority of cases were also more likely to ever use alcohol (P=0.004). In contrast, lower percentages of cases had hypertension (P=0.04). Prevalence of diabetes was similar in both groups (P=0.09). Regarding BMI at diagnosis, nearly 52% of the subjects were overweight or obese (i.e., had a BMI≥25 kg/m^2). A higher percentage of cases were obese compared to controls (P=0.05).

Table 2 describes the tumor characteristics and treatment by case and control status. Cases were more likely to have higher stage tumors (P<0.001), have a Gleason score of 8+, higher tumor grade, more positive lymph nodes, and higher PSA levels at diagnosis (P<0.05 for all variables) than controls. As expected, fatal cases were more likely to have higher grade tumors (P<0.001). Regarding treatment, cases were more likely to undergo radiotherapy for curative intent following prostatectomy (P<0.001), however, we found no difference by case and control status regarding use of neoadjuvant hormone treatment (which was not widely

used) nor receipt of additional curative treatment >6 months post diagnosis. When we further compared tumor characteristics and treatment stratified by case-control status and BMI, more overweight/obese cases had higher Gleason score (P=0.03), positive surgical margins (P<0.0001), positive lymph nodes (P=0.02), and higher tumor grade of 3 (difference not statistically significant) than overweight/obese controls (Table 3).

The results of overall and multivariable unconditional logistic regression (based on the matched sets) are presented in Table 4 stratified by Gleason score. In addition to the matching variables, we also adjusted for PSA at diagnosis, surgical margins, tumor grade, lymph node status, and adjuvant radiotherapy. Overall, men who died from prostate cancer were 1.5 times more likely to be obese at diagnosis when compared to men who did not die from prostate cancer (adjusted OR: 1.55, 95% CI: 1.05, 2.28) (Table 4). For comparison, adjusted OR for this analysis obtained via conditional logistic regression was 1.62, 95% CI: 1.08, 2.44). Gleason score modified the association between BMI at diagnosis and prostate cancer mortality. After stratifying by Gleason score, the odds of mortality generally rose with increasing BMI. The highest effect measure was observed in the Gleason Score 8+ category (AOR=2.45, 95% CI: 1.11–5.42). These associations persisted after adjusting for PSA at diagnosis.

DISCUSSION

In this population based study, fatal prostate cancer was strongly associated with being overweight or obese at diagnosis, and further, this association was stronger in men with higher Gleason scores. Of note, the effect of BMI on prostate cancer mortality was independent of treatment in addition to radical prostatectomy, PSA at diagnosis, surgical margin status, lymph node status, and other clinical or patient factors we examined. Because the majority of the fatal cases were initially diagnosed with early stage disease (82%, TNM stage II–III), our results suggest that behavioral interventions to reduce weight might help prolong survival.

Our results are concordant with previous studies which determined that BMI at or near diagnosis were associated with increased prostate cancer deaths [11, 20–21]. Also, previous studies suggest that BMI is associated with more aggressive disease [22,23]. Our results support these findings in that the highest risk of prostate cancer mortality was seen among obese men with aggressive disease (Gleason score >8). Moreover, the magnitude of the effect of BMI on prostate cancer mortality (particularly in obese or overweight men with Gleason scores 8+) is similar or greater than those reported of clinical trials that compared mortality risks in patients who underwent surgery versus active surveillance [24].

Obesity may influence prostate cancer prognosis in various ways. Molecular studies have delineated metabolic pathways related to insulin signaling and lipid deregulation that may directly foster cancer development [25]. In addition, obesity increases the prostate cancer recurrence [21,24,26], and may also negatively influence prostate cancer outcomes by potentially delaying prostate cancer detection [27–28]. Also, it is plausible that obesity's influence on testosterone levels and growth factors may contribute to its effect on prostate cancer aggressiveness and mortality. Obese men have lower testosterone levels, which may

predispose them to more aggressive disease [29–30]. Also, growth factors such as insulin growth factor-1 (IGF-1) and adipocytes are increased among obese men and are associated with carcinogenesis [31–32]. Taken together, the combination of promoting aggressive carcinogenesis, delaying detection, increasing risk of positive surgical margins (due to difficulty of surgery), and increasing risk of recurrence may all contribute to an increased risk of prostate cancer mortality among obese men. Additionally, higher BMI may be a surrogate marker for other factors associated with poor prostate cancer outcomes, such as lower physical activity or poor diet.

This study comprehensively evaluated the association between BMI and prostate cancer mortality using electronic medical record data and a large number of verified prostate cancer deaths. It utilized a diverse population of men who were long-term members of health maintenance organizations and thus had equivalent access to health care. However, in addition to these strengths, there are potential limitations that need to be considered. BMI may not be the most accurate way to measure obesity; however, height and weight were collected via medical record and not self-report, thus limiting the potential for recall bias. We did not collect information on prostate volume, which could have been larger in obese men. However, this factor is associated with stage and because we matched on stage, the confounding effect of prostate volume is minimized. Although the study covered only insured men, the memberships of these organizations broadly reflect the general population in California and Oregon in terms of race/ethnicity and sociodemographic characteristics. Because this study was conducted on men who underwent radical prostatectomy, generalizing to other treatment groups (e.g., active surveillance, radiation) should be done with caution. Although we did not adjust for cardiovascular disease, we did examine risk factors of cardiovascular disease in the analysis. Further, although the number of incident prostate cancer cases was high in this health plans (roughly 3,000 men were diagnosed with the disease annually), the paucity of deaths due to the disease limited the number of eligible cases for our study. Hence, larger studies with prostate cancer deaths are needed to confirm our findings. Finally, because this was an observational study, inferences regarding causality may be limited. However, we had uniform access to all data on nearly all eligible subjects.

In conclusion, results for this study suggest that obese men are more likely to die from prostate cancer when compared to non-obese men and this association is strongest among men with higher Gleason scores. Because the majority of the fatal cases were diagnosed at early stage disease, future studies are needed to determine the optimal lifestyle modifications, such as diet or physical activity that could prolong survival.

Acknowledgments

Sources of Funding:

This study was supported by U.S. National Institutes of Health/National Cancer Institute Grant R01CA100743 (SW). The funding agency had no role in the design, collection, analysis or interpretation of the results.

References

1. American Cancer Society. Cancer Facts & Figures 2010. Atlanta: American Cancer Society; 2010.

2. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. 2010; 303:235–41. [PubMed: 20071471]
3. Amling CL, Riffenburgh RH, Sun L, Moul JW, Lance RS, Kusuda L, et al. Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. J Clin Oncol. 2004; 22:439–45. [PubMed: 14691120]
4. Bassett WW, Cooperberg MR, Sadetsky N, Silva S, DuChane J, Pasta DJ, et al. Impact of obesity on prostate cancer recurrence after radical prostatectomy: data from CaPSURE. Urology. 2005; 66:1060–5. [PubMed: 16286124]
5. Freedland SJ, Aronson WJ, Kane CJ, Presti JC Jr, Amling CL, Elashoff D, 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. J Clin Oncol. 2004; 22:446–53. [PubMed: 14691122]
6. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. Nat Rev Cancer. 2004; 4:579–91. [PubMed: 15286738]
7. MacInnis RJ, English DR. Body size and composition and prostate cancer risk: systematic review and meta-regression analysis. Cancer Causes Control. 2006; 17:989–1003. [PubMed: 16933050]
8. MacInnis RJ, English DR, Gertig DM, Hopper JL, Giles GG. Body size and composition and prostate cancer risk. Cancer Epidemiol Biomarkers Prev. 2003; 12:1417–21. [PubMed: 14693731]
9. Parr CL, Batty GD, Lam TH, Barzi F, Fang X, Ho SC, et al. Body-mass index and cancer mortality in the Asia-Pacific Cohort Studies Collaboration: pooled analyses of 424,519 participants. Lancet Oncol. 2010; 11:741–52. [PubMed: 20594911]
10. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008; 371:569–78. [PubMed: 18280327]
11. Rodriguez C, Patel AV, Calle EE, Jacobs EJ, Chao A, Thun MJ. Body mass index, height, and prostate cancer mortality in two large cohorts of adult men in the United States. Cancer Epidemiol Biomarkers Prev. 2001; 10:345–53. [PubMed: 11319175]
12. 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; 54:884–90. [PubMed: 10565752]
13. Freedland SJ, Humphreys EB, Mangold LA, Eisenberger M, Dorey FJ, Walsh PC, et al. Risk of prostate-cancer specific mortality following biochemical recurrence after radical prostatectomy. JAMA. 2005; 294:433–9. [PubMed: 16046649]
14. Gong Z, Agalliu I, Lin DW, Stanford JL, Kristal AR. Obesity is associated with increased risks of prostate cancer metastasis and death after initial cancer diagnosis in middle-aged men. Cancer. 2007; 109:1192–202. [PubMed: 17311344]
15. National Heart Lung Blood Institute. [Accessed October 1, 2012] http://nhlbisupport.com/bmi/
16. World Health Organization. [Accessed May 20, 2013] http://apps.who.int/bmi/index.jsp?introPage=intro_3.html
17. Prentice R. Use of the logistic model in retrospective studies. Biometrics. 1976; 32:599–606. [PubMed: 963173]
18. Lynn HS, McCulloch CE. When does it pay to break the matches for analysis of a matched-pairs design? Biometrics. 1992; 48:397–409. [PubMed: 1637969]
19. Breslow, NE.; Day, NE. Statistical methods in cancer research: the analysis of case-control studies. IARC Sci Publ; 1980. p. 5-338.
20. Freedland SJ, Bañez LL, Sun LL, Fitzsimons NJ, Moul JW. Obese men have higher-grade and larger tumors: an analysis of the duke prostate center database. Prostate Cancer Prostatic Dis. 2009; 12:259–63. [PubMed: 19581922]
21. 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; 4:486–501. [PubMed: 21233290]
22. Rodriguez C, Freedland SJ, Deka A, Jacobs EJ, McCullough ML, Patel AV, et al. Body mass index, weight change, and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiol Biomarkers Prev. 2007; 16:63–9. [PubMed: 17179486]

23. Gong Z, Neuhouser ML, Goodman PJ, Albanes D, Chi C, Hsing AW, et al. Obesity, diabetes, and risk of prostate cancer: results from the prostate cancer prevention trial. Cancer Epidemiol Biomarkers Prev. 2006; 15:1977–83. [PubMed: 17035408]
24. Bill-Axelson A, Holmberg L, Filén F, Ruutu M, Garmo H, Busch C, et al. Radical prostatectomy versus watchful waiting in localized prostate cancer: the Scandinavian prostate cancer group-4 randomized trial. J Natl Cancer Inst. 2008; 100:1144–54. [PubMed: 18695132]
25. Khandekar MJ, Cohen P, Spiegelman BM. Molecular mechanisms of cancer development in obesity. Nat Rev Cancer. 2011; 11:886–95. [PubMed: 22113164]
26. Bassett WW, Cooperberg MR, Sadetsky N, Silva S, DuChane J, Pasta DJ, et al. Impact of obesity on prostate cancer recurrence after radical prostatectomy: data from CaPSURE. Urology. 2005; 66:1060–5. [PubMed: 16286124]
27. Freedland SJ, Humphreys EB, Mangold LA, Eisenberger M, Partin AW. Time to prostate specific antigen recurrence after radical prostatectomy and risk of prostate cancer specific mortality. J Urol. 2006; 176 (4 Pt 1):1404–8. [PubMed: 16952644]
28. Wallner LP, Morgenstern H, McGree ME, Jacobson DJ, St Sauver JL, Jacobsen SJ, et al. The effects of body mass index on changes in prostate-specific antigen levels and prostate volume over 15 years of follow-up: implications for prostate cancer detection. Cancer Epidemiol Biomarkers Prev. 2011; 20:501–8. [PubMed: 21242331]
29. Massengill JC, Sun L, Moul JW, Wu H, McLeod DG, Amling C, et al. Pretreatment total testosterone level predicts pathological stage in patients with localized prostate cancer treated with radical prostatectomy. J Urol. 2003; 169:1670–5. [PubMed: 12686805]
30. Schatzl G, Madersbacher S, Thurridl T, Waldmüller J, Kramer G, Haitel A, et al. High-grade prostate cancer is associated with low serum testosteronelevels. Prostate. 2001; 47:52–8. [PubMed: 11304729]
31. Rowlands MA, Gunnell D, Harris R, Vatten LJ, Holly JM, Martin RM. Circulating insulin-like growth factor peptides and prostate cancer risk: a systematic reviewand meta-analysis. Int J Cancer. 2009; 124:2416–29. [PubMed: 19142965]
32. Rowlands MA, Holly JM, Gunnell D, Donovan J, Lane JA, Hamdy F, et al. Circulating insulin-like growth factors and IGF-binding proteins in PSA-detected prostate cancer: the large case-control study ProtecT. Cancer Res. 2012; 72:503–15. [PubMed: 22106399]

Table 1

Characteristics of the Study Groups

	Cases N=323 (N, %)	Controls N=428 (N, %)
Health Plan		
KPNW	37 (11%)	38 (9%)
KPNC	152 (47%)	190 (44%)
KPSC	134 (41%)	200 (47%)
	P=0.27	
Years in health plan before diagnosis		
< 5 years	58 (18%)	24 (6%)
≥ 5 years	252 (78%)	351 (82%)
Missing	13 (4%)	53 (12%)
	P <0.0001	
Age at diagnosis, y		
48–59	78 (24%)	98 (23%)
60–64	75 (23%)	108 (25%)
65–69	102 (32%)	142 (33%)
70–81	68 (21%)	79 (18%)
Missing	0 (0%)	1 (0.2%)
	P=0.78	
Race		
Caucasian	277 (86%)	331 (77%)
Non-Caucasian	46 (14%)	97 (23%)
	P=0.004	
Year of diagnosis		
1971–1984	26 (8%)	27 (6%)
1985–1989	87 (27%)	91 (21%)
1990–1994	163 (50%)	230 (54%)
1995–2001	47 (15%)	80 (19%)
	P=0.14	
Symptomatic at diagnosis		
Yes	196 (61%)	211 (49%)
No	124 (38%)	215 (50%)
Missing	3 (1%)	1 (0.2%)
	P=0.003	
Prior BPH but not symptomatic at diagnosis		
Yes	44 (14%)	69 (16%)
No	279 (86%)	359 (84%)
	P=0.34	
TNM Stage at diagnosis		
2	98 (30%)	217 (51%)
3	168 (52%)	174 (41%)

	Cases N=323 (N, %)	Controls N=428 (N, %)
4	57 (18%)	37 (9%)
	P=<0.0001	
Personal history of cancer		
Yes	29 (9%)	70 (16%)
No	292 (90%)	358 (84%)
Missing	2 (1%)	0 (0%)
	P=0.004	
History of hypertension (co-morbidity)		
Yes	156 (48%)	234 (55%)
No	167 (52%)	194 (45%)
	P=0.08	
History of diabetes (co-morbidity)		
Yes	41 (13%)	75 (18%)
No	282 (87%)	353 (82%)
	P=0.07	
History of tobacco use		
Ever	189 (59%)	228 (53%)
Never	125 (39%)	191 (45%)
Missing	9 (3%)	9 (2%)
	P=0.25	
History of alcohol use		
Ever	209 (65%)	245 (57%)
Never	94 (29%)	162 (38%)
Missing	20 (6%)	21 (5%)
	P=0.04	
BMI (kg/m^2)		
Normal (18.5–24.9)	64 (20%)	109 (25%)
Overweight (25–29.9)	162 (50%)	226 (53%)
Obese (30+)	97 (30%)	93 (22%)
	P=0.02	

Table 2

Tumor Characteristics & Cancer Treatment

	Case (N, %)	Control (N, %)
Gleason score		
<7	19 (6%)	123 (29%)
7	157 (49%)	188 (44%)
8+	126 (39%)	41 (10%)
Missing	21 (6%)	76 (17%)
	P<0.0001	
Tumor grade		
1	4 (1%)	7 (2%)
2	37 (11%)	153 (36%)
3	282 (88%)	262 (61%)
Missing	0 (0%)	6 (1%)
	P<0.0001	
Positive Margins		
Yes	146 (45%)	154 (36%)
No	149 (46%)	197 (46%)
Missing	28 (9%)	77 (18%)
	P<0.0001	
Lymph nodes		
Yes	44 (14%)	29 (7%)
No	211 (65%)	272 (64%)
Missing	68 (21%)	127 (29%)
	P<0.0001	
PSA at diagnosis		
0–6	59 (18%)	86 (20%)
7–10	50 (15%)	101 (24%)
11–18	57 (18%)	93 (22%)
19+	77 (24%)	70 (16%)
Missing	80 (25%)	78 (18%)
	P=0.002	
Curative txt >6 months after diagnosis		
Yes	222 (69%)	285 (67%)
No	101 (31%)	143 (33%)
	P=0.73	
Radiation txt for curative intent plus prostatectomy		
Yes	99 (31%)	65 (15%)
No	224 (69%)	363 (85%)
	P<0.0001	
Neoadjuvant hormone treatment		
Yes	18 (6%)	19 (4%)

	Case (N, %)	Control (N, %)
No	305 (94%)	409 (96%)
	P=0.48	

Table 3

Tumor Characteristics and Cancer Treatment by BMI status

Tumor Characteristics and Cancer Treatment	Cases		Controls		
	Healthy (18.5–24.9) N (%)	Overweight/Obese (≥25) N (%)	Healthy (18.5–24.9) N (%)	Overweight/Obese (≥25) N (%)	P-Value (Chi-Square)
Total	**64**	**259**	**109**	**319**	
Gleason Score					
<7	6 (32%)	13 (68%)	34 (28%)	89 (72%)	0.72
7	25 (16%)	132 (84%)	43 (23%)	146 (77%)	0.11
8+	28 (22%)	98 (78%)	16 (39%)	25 (61%)	0.03
Missing	5 (24%)	16 (76%)	16 (21%)	60 (79%)	0.79
Tumor grade					
1	0 (0%)	4 (100%)	1 (14%)	6 (86%)	0.43
2	8 (22%)	29 (78%)	41 (27%)	112 (73%)	0.52
3	56 (20%)	226 (80%)	67 (25%)	198 (75%)	0.13
Missing	0 (0%)	0 (0%)	0 (0%)	3 (100%)	
Positive Margins					
Yes	18 (12%)	128 (88%)	42 (27%)	112 (73%)	0.001
No	39 (26%)	110 (74%)	50 (25%)	148 (75%)	0.85
Missing	7 (25%)	21 (75%)	17 (22%)	60 (78%)	0.75
Lymph nodes					
Yes	6 (14%)	38 (86%)	11 (38%)	18 (62%)	0.02
No	44 (21%)	167 (79%)	68 (25%)	204 (75%)	0.28
Missing	14 (21%)	54 (79%)	30 (24%)	97 (76%)	0.63
PSA at diagnosis					
0–6	12 (20%)	47 (80%)	14 (16%)	72 (84%)	0.53
7–10	5 (10%)	45 (90%)	35 (35%)	66 (65%)	0.001
11–18	11 (19=%)	46 (81%)	25 (27%)	68 (73%)	0.29
19+	20 (26%)	57 (74%)	17 (24%)	53 (76%)	0.81
Missing	16 (20%)	64 (80%)	18 (23%)	60 (77%)	0.64
Stage at diagnosis					

Tumor Characteristics and Cancer Treatment	Cases		Controls		
	Healthy (18.5–24.9)	Overweight/Obese (≥25)	Healthy (18.5–24.9)	Overweight/Obese (≥25)	P-Value (Chi-Square)
	N (%)	N (%)	N (%)	N (%)	
Total	**64**	**259**	**109**	**319**	
2	14 (14%)	84 (86%)	54 (25%)	163 (75%)	0.03
3	40 (24%)	128 (76%)	42 (24%)	132 (76%)	0.94
4	10 (18%)	47 (82%)	13 (35%)	24 (65%)	0.05
Primary Treatment					
Curative treatment > 6 months after diagnosis					
Yes	47 (21%)	175 (79%)	69 (24%)	216 (76%)	0.42
No	17 (17%)	84 (83%)	40 (28%)	103 (72%)	0.04
Radiation-curative intent					
Yes	15 (15%)	84 (85%)	10 (15%)	55 (85%)	0.97
No	49 (22%)	175 (78%)	99 (27%)	264 (73%)	0.14
ADT					
Yes	3 (17%)	15 (83%)	5 (26%)	14 (74%)	0.48
No	61 (20%)	244 (80%)	104 (25%)	305 (75%)	0.09
Radiation without ADT	13 (14%)	82 (86%)	8 (13%)	53 (87%)	0.92
Radiation with ADT	2 (50%)	2 (50%)	2 (50%)	2 (50%)	1.00

Table 4

Association between BMI & Prostate Cancer Mortality by Gleason Score

	Cases N (%)	Controls N (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Gleason Score < 7				
Healthy BMI (0–24.9)	6 (33.3)	31 (27.0)	referent	referent
Overweight/Obese (BMI>25)	12 (66.7)	84 (73.0)	0.74 (0.25, 2.14)	1.41 (0.43, 4.62)
Gleason Score = 7				
Healthy BMI (0–24.9)	22 (15.2)	41 (23.6)	referent	referent
Overweight/Obese (BMI>25)	123 (84.8)	133 (76.4)	1.72 (0.97, 3.06)	1.49 (0.84, 2.64)
Gleason Score = 8+				
Healthy BMI (0–24.9)	25 (21.7)	15 (40.5)	referent	referent
Overweight/Obese (BMI>25)	90 (78.3)	22 (59.5)	2.45 (1.11, 5.42)	2.06 (0.93, 4.59)
Overall				
Healthy BMI (0–24.9)	53 (19.1)	87 (26.7)	referent	referent
Overweight/Obese (BMI>25)	225 (80.9)	239 (73.3)	1.87 (1.15, 3.05)	1.55 (1.05, 2.28)

*Adjusted unconditional multivariate models accounted for the following matching factors (health plan site, race, age at diagnosis, year of diagnosis, stage at diagnosis, duration of health plan membership) and other significant covariates (PSA at diagnosis, surgical margins status, and lymph node status).