Research Article

Cancer Prevention Research

Weight Gain Is Associated with an Increased Risk of Prostate Cancer Recurrence after Prostatectomy in the PSA Era

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Abstract

Although obesity at the time of prostatectomy has been associated with prostate cancer recurrence, it is unknown whether obesity before or after surgery, or weight change from the years prior to surgery to after surgery is associated with recurrence. Thus, we examined the influence of obesity and weight change on recurrence after prostatectomy. We conducted a retrospective cohort study of 1,337 men with clinically localized prostate cancer who underwent prostatectomy performed during 1993–2006 by the same surgeon. Men self-reported weight and physical activity at 5 years before and 1 year after surgery on a survey during follow-up. Mean follow-up was 7.3 years. We estimated multivariable-adjusted HRs of prostate cancer recurrence comparing obesity at 5 years before and at 1 year after surgery with normal weight, and a gain of more than 2.2 kg from 5 years before to 1 year after surgery with stable weight. During 9,797 person years of follow-up, 102 men recurred. Compared with men who had stable weight, those whose weight increased by more than 2.2 kg had twice the recurrence risk (HR = 1.94; 95% CI, 1.14–3.32) after taking into account age, pathologic stage and grade, and other characteristics. The HR of recurrence was 1.20 (95% CI, 0.64–2.23) and 1.72 (95% CI, 0.94–3.14) comparing obesity at 5 years before and at 1 year after surgery, respectively, with normal weight. Physical activity (≥5 h/wk) did not attenuate risk in men who gained more than 2.2 kg. By avoiding weight gain, men with prostate cancer may both prevent recurrence and improve overall well-being. *Cancer Prev Res; 4(4); 544–51. ©2011 AACR.*

Introduction

Approximately 20% of men with clinically localized prostate cancer who undergo radical prostatectomy recur within 10 years postsurgery (1). Currently, there are no evidence-based recommendations for men to reduce their risk of recurrence after treatment. Focusing on modifiable factors may provide opportunities for men with prostate cancer to prevent recurrence and improve their overall well-being through behavior change.

Obesity measured at or near the time of treatment for early-stage prostate cancer has been associated with increased risk of recurrence in most (2–15), but not all, studies (16–19). Obesity has also been associated with high-grade disease at diagnosis, and the development of advanced or fatal prostate cancer, but not total prostate cancer incidence (20–23). However, the relevant timing of obesity (e.g., before or after diagnosis) to risk of prostate cancer recurrence has not been established. Further, whether weight change influences risk is largely unstudied. Weight gain between young adulthood and time of diagnosis was associated with prostate cancer recurrence in one prospective study, though, the analysis did not account for important clinical and pathologic factors that may have confounded the association (8). Determining the relevant timing of obesity and understanding the effect of weight change on prostate cancer recurrence are necessary to both elucidate the mechanism by which adiposity influences risk and to develop strategies to prevent recurrence.

Physical inactivity may exacerbate the obesity-related risk of prostate cancer recurrence, though this relationship has

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not been explored. Although studies of physical activity and prostate cancer incidence have been inconsistent overall (24), several of the recent large studies suggest at least some benefit of increased physical activity on prostate cancer risk (25–27).

We investigated the association of obesity 5 years before and 1 year after prostatectomy, as well as weight change during this time period with prostate cancer recurrence in a retrospective cohort study. We selected the interval of 5 years before surgery to 1 year after surgery to capture the possible influence of weight gain on cancer cells that may have escaped from the primary tumor before surgery. We also assessed both the independent and modifying effects of physical inactivity, an obesity-related behavior.

Methods

Study population

We conducted a retrospective cohort study of men with clinically localized prostate cancer who underwent radical retropubic prostatectomy performed by the same surgeon at Johns Hopkins Hospital between January 1, 1993, and March 31, 2006 ($n = 2{,}498$). Those who underwent previous hormone or radiation therapy were excluded (1.2%). For all men eligible for this study, electronic or paper medical records were reviewed by one abstractor (A.M.M.) who was blinded to recurrence status. Information on age, race/ethnicity, first degree family history of prostate cancer, preoperative prostate-specific antigen (PSA), surgery year, positive surgical margins, pathologic stage, and Gleason sum was abstracted from the medical records. Men alive and residing in the United States as of November 2007 were mailed a survey on dietary, lifestyle, and medical factors ($n = 2{,}111$). This analysis included men who responded to the survey as of August 2009 and had complete information on height, weight, and physical activity ($n = 1{,}337$). Men were followed for recurrence through August 2009, with mean follow-up time of 7.3 years. The follow-up of this cohort was approved by the Institutional Review Board at the Johns Hopkins School of Medicine. This analysis was additionally approved by the Institutional Review Board at the Johns Hopkins Bloomberg School of Public Health.

Exposure assessment

In the survey, the men self-reported their weight and physical activity level at 5 years before surgery and 1 year after surgery. In this retrospective study, we chose to evaluate 1 year after surgery, as opposed to at the time of surgery, to avoid weight and behavior change specifically related to diagnosis and treatment of the initial prostate cancer.

We calculated body mass index (BMI) using height and weight data, and classified men as normal (<25 kg/m^2), overweight (25–29.9 kg/m^2), or obese ($\geq$30 kg/m^2). Weight change was defined as the difference in self-reported weight at 5 years before surgery and 1 year after surgery. To capture physical activity, men were asked the number of hours per week they spent "doing leisure time physical activity (walking, running, lap swimming, bicycling, and other sports)." Physical activity at 5 years before surgery and at 1 year after surgery were categorized into tertiles for primary analyses (<4, 4–6, and $\geq$7 h/wk). For stratified analyses, physical activity at 1 year after surgery was divided at the median value ($\geq$5 h/wk as physically active, <5 h/wk inactive). Men were asked whether they had ever received a diagnosis of diabetes from a doctor and the month and year of the diagnosis. Men were classified as having been diagnosed before or after surgery (but before recurrence).

Outcome assessment

Men were evaluated by their primary care physicians with PSA tests and digital-rectal examinations every 3 months for the first year postoperative, semiannually for the second year, and annually thereafter. Recurrence was defined as confirmed PSA re-elevation to 0.2 ng/mL or more above a nadir of nondetectable, local recurrence, metastasis, or death from prostate cancer. Annually, the surgeon contacted the men to request that their physicians send their most recent PSA test results. Elevated tests were repeated by the surgeon. PSA information was complete for 99% and 78% of the men at 1 and 5 years after surgery, respectively. Prostate cancer death was obtained through family report or linkage with the National Death Index. Of the 102 men who recurred, 11% had metastases or died from prostate cancer.

Statistical analysis

We calculated age-adjusted means and proportions for demographic and other factors by BMI 5 years before surgery and weight change by using regression modeling. Men began contributing time at risk starting 1 year after surgery. Cases were men who recurred after the first year postsurgery. We used Cox proportional hazards regression to estimate the HR of recurrence for obesity and physical activity at 5 years before surgery and at 1 year after surgery, and weight change. Weight change was modeled in two ways. First, we used indicator variables for weight loss and gain with maintenance as the reference, defined as a weight change of 2.2 kg or less, to allow for minor weight fluctuation. Second, to avoid subjective cutpoints and assess the shape of the association, continuous weight change was modeled by using restricted quadratic splines with knots at the 10th, 50th, and 90th percentiles of the distribution. The top and bottom 1% of the distribution of weight change were excluded from the restricted quadratic splines model to avoid the influence of extreme values. To test whether the association between weight gain and recurrence was consistent with a linear dose–response, we used the likelihood ratio test to compare the linear and spline models. We confirmed the proportional hazards assumption for all models by including an interaction term between the main effect and follow-up time in the model and testing the coefficient by using the Wald test. All models were compatible with the proportional hazards assumption. To test for trend across levels of BMI, physical activity, and weight

change, we assigned each man the median value within his category of weight. The median values were modeled and the coefficient was tested with the Wald test. To explore whether physical activity level modified the association of obesity and weight gain with recurrence risk, we stratified the analysis by physical activity level.

Three primary analyses were performed for obesity and physical activity: (a) adjusted for age; (b) adjusted for age and nonmodifiable risk factors including race/ethnicity, family history, year of prostatectomy, and pathologic stage and grade; and (c) adjusted for all covariates in the previous models plus modifiable risk factors including cigarette smoking status, and mutual adjustment for physical activity and BMI in the same time period. Because weight at 5 years before surgery and weight change were correlated, to determine the independent association for weight change and recurrence, we adjusted for weight at 5 years before surgery and height along with the nonmodifiable factors (listed in (b) above), cigarette smoking status, and physical activity. In the primary analyses, diabetes did not seem to be a confounder and thus was not included in the models. In subanalyses, we further adjusted for preoperative PSA, excluded men with positive surgical margins, and excluded men with diabetes. All analyses were conducted by SAS version 9.1 (Cary, NC). All tests were 2-sided and results were considered statistically significant if $P < 0.05$.

Results

At 5 years before prostatectomy, approximately 53% of men were overweight and 9% were obese. The men who were obese were also less active 5 years before surgery, and more likely to be former smokers and to report a diagnosis of diabetes (Table 1). After pathologic review, obese men were less likely to have organ-confined disease and more likely to have positive surgical margins. Between 5 years before surgery and 1 year after surgery, 13.9% of men gained more than 2.2 kg and 12.7% of men lost more than 2.2 kg. Men who gained weight were younger and more likely to be current smokers (Table 1). Men who lost weight were more likely to be diabetic. Compared with men who maintained their weight, men who lost weight had a higher BMI and were less active at 5 years before prostatectomy. Pathologic characteristics did not differ among categories of weight change.

Men who were obese at 5 years before prostatectomy seemed to have an increased age-adjusted risk of prostate cancer recurrence compared with normal-weight men; though this association was not statistically significant and was attenuated in the multivariable models (Table 2). Overweight men did not have an increased risk of recurrence as compared with normal-weight men. Likewise, physical inactivity at 5 years before prostatectomy was not associated with risk of prostate cancer recurrence.

Obesity at 1 year after surgery was associated with a 2-fold increase in risk of prostate cancer recurrence as compared with normal-weight men after adjustment for age. After multivariable adjustment, the association was modestly attenuated, and no longer statistically significant. In subanalyses, nonstatistically significant positive associations between obesity at 1 year after surgery and recurrence were observed with additional adjustment for presurgery PSA (multivariable-adjusted HR = 1.64; 95% CI, 0.89–3.03), after exclusion of men with positive surgical margins (HR = 1.59; 95% CI, 0.81–3.13) and after exclusion of men with diabetes (HR = 1.50; 95% CI, 0.78–2.87). Physical inactivity at 1 year after prostatectomy was not associated with an increased risk of prostate cancer recurrence; this association did not change in subanalyses further adjusting for presurgery PSA, excluding men with positive surgical margins, or excluding men with diabetes (data not shown).

Men who gained weight were at a nearly 2-fold increased risk of prostate cancer recurrence when compared with men who maintained their weight; this result was statistically significant (Table 3). Men who lost weight seemed to have a lower risk of prostate cancer recurrence, though the association was not statistically significant. When the association between weight change and recurrence was modeled by using restricted quadratic splines, the risk of prostate cancer recurrence increased with increasing weight gain, whereas risk seemed to decrease with weight loss (Fig. 1). This association was statistically consistent with a linear dose–response. In subanalyses, there was a similar association between weight gain and recurrence with additional adjustment for presurgery PSA (HR = 1.85; 95% CI, 1.07–3.20) and when men with diabetes were excluded (HR = 1.90; 95% CI, 1.10–3.29); although the association was attenuated when men with positive surgical margins were excluded (HR = 1.47; 95% CI, 0.80–2.69). The association between weight change and recurrence did not differ by BMI (<25, ≥ 25 kg/m^2) at 5 years before surgery (data not shown).

Among inactive men, obesity at 1 year after surgery was associated with a nearly 2-fold increased risk of prostate cancer recurrence, though not statistically significant (Table 4), whereas the association for obesity 1 year after surgery was attenuated among active men. Physical inactivity did not modify the elevated risk of recurrence in men who gained weight; the risk of recurrence was higher in men who gained weight irrespective of physical activity level (Table 4).

Discussion

In this retrospective cohort study, weight gain from 5 years before prostatectomy to 1 year after was associated with a nearly 2-fold increased risk of prostate cancer recurrence. This association remained significant even among physically active men. Further, there seemed to be a linear association between weight change and recurrence, suggesting that risk of recurrence increased with increasing weight gain, and decreased with increasing weight loss.

Obesity and weight gain may influence risk of prostate cancer recurrence through several mechanisms, including metabolic, hormonal, and inflammatory pathways. Obese men tend to have higher insulin and leptin levels and lower

Table 1. Age-adjusted demographic and pathologic tumor characteristics by BMI 5 years before prostatectomy and weight change[a]

	BMI (kg/m^2)				Weight Change (>2.2 kg)			
	<25.0 ($n = 503$)	25.0–29.9 ($n = 716$)	≥30.0 ($n = 118$)	*P*	Loss ($n = 170$)	Maintenance ($n = 981$)	Gain ($n = 186$)	*P*
Mean age (SD)	56.4(6.8)	56.4(6.5)	57.0(6.3)	0.66	57.0(6.1)	56.8(6.5)	53.9(6.9)	<0.001
Race/ethnicity (%)								
White	95.6	94.4	95.7		94.7	94.9	95.9	
Black	0.6	2.5	2.6	0.14	0.0	2.0	2.5	0.91
Other/missing	3.8	3.1	1.7		5.3	3.2	1.6	
Family history of prostate cancer (%)								
No	66.1	67.9	66.5		70.1	66.2	69.3	
Yes	27.3	26.1	27.6	0.97	21.1	27.9	25.4	0.27
Missing	6.6	6.0	5.8		8.7	5.9	5.3	
Smoking status, %								
Never	57.8	50.4	46.8		42.6	55.9	46.0	
Former	38.6	45.8	53.1	0.04	54.9	40.7	49.5	<0.01
Current	2.0	2.5	0		1.2	2.1	2.9	
Missing	1.6	1.3	0		1.2	1.2	1.6	
Mean preoperative PSA (SE)	6.4(0.2)	6.7(0.2)	6.6(0.4)	0.52	6.8(0.3)	6.5(0.1)	6.9(0.3)	0.36
Median surgery year	1999.2	1999.1	1999.4	0.77	1999.5	1999.1	1999.7	0.07
Mean pathologic Gleason sum (SE)	6.3(0.03)	6.3(0.02)	6.4(0.06)	0.17	6.3(0.05)	6.3(0.02)	6.3(0.05)	0.72
Pathologic stage, %								
Organ-confined	78.7	73.7	59.6		71.6	74.9	73.9	
Focal or established capsular penetration	17.7	22.5	35.3	0.001	23.8	21.8	20.4	0.60
Seminal vesicle or lymph node positive	3.4	3.8	4.2		4.6	3.2	5.1	
Positive surgical margins, %	4.4	6.4	11.8	0.01	7.6	6.2	4.7	0.54
Diabetes mellitus diagnosis, %								
Never	98.6	96.8	84.8		90.6	97.4	96.6	
Before prostatectomy	0.6	1.5	9.3	0.001	4.7	1.4	1.7	<0.01
After prostatectomy	0.8	1.7	5.9		4.7	1.2	1.7	
BMI, kg/m^2								
Mean 5 years before prostatectomy (SE)	23.2(0.06)	26.8(0.05)	32.4(0.1)	<0.001	28.8(0.2)	25.4(0.09)	26.3(0.2)	<0.001
Mean 1 year after prostatectomy (SE)	23.4(0.08)	27.0(0.06)	31.2(0.2)	<0.001	26.7(0.2)	25.5(0.09)	28.1(0.2)	<0.001
Mean weight change, kg (SE)	0.6(0.2)	0.4(0.1)	−3.6(0.3)	<0.001	-6.6(0.2)	0.3(0.07)	5.7(0.2)	<0.001
Physical activity, h/wk								
Mean 5 years before prostatectomy (SE)	7.1(0.3)	6.7(0.2)	5.3(0.6)	0.01	5.6(0.5)	6.8(0.2)	7.5(0.5)	0.01
Mean 1 year after prostatectomy (SE)	7.0(0.3)	6.6(0.2)	6.3(0.6)	0.32	6.6(0.5)	6.8(0.2)	6.3(0.5)	0.50

[a]Characteristics of 1,337 men undergoing radical prostatectomy at Johns Hopkins Hospital 1993–2006.

androgen levels (23). These metabolic and hormonal changes may differ throughout the natural history of weight change. The consequences of these adipose-mediated metabolic and hormonal changes may influence prostate cancer differently depending on when they occur during the natural history of prostate cancer carcinogenesis: before disease is present, early in the natural history, or after detection or treatment. We focused on the time frame

Table 2. Association of BMI and physical activity 5 years before and 1 year after prostatectomy with prostate cancer recurrence

	5 Years before prostatectomy[a]					1 Year after prostatectomy[a]				
	Cases/total	Person years	Age-adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)[b]	Multivariable-adjusted HR (95% CI)[c]	Cases/total	Person years	Age-adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)[b]	Multivariable-adjusted HR (95% CI)[c]
BMI, kg/m^2										
<25.0	40/503	3,686	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	35/497	3,690	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
25.0–29.9	47/716	5,289	0.82 (0.54–1.25)	0.76 (0.50–1.16)	0.73 (0.47–1.13)	50/721	5,266	1.00 (0.65–1.54)	0.92 (0.60–1.43)	0.89 (0.57–1.38)
≥30.0	15/118	822	1.64 (0.91–2.98)	1.27 (0.69–2.33)	1.20 (0.64–2.23)	17/119	841	2.17 (1.22–3.88)	1.78 (0.98–3.21)	1.72 (0.94–3.14)
Test for trend[d]			0.27	0.71	0.84			0.02	0.10	0.13
Physical activity, h/wk										
<4	28/405	2,966	0.95 (0.59–1.55)	0.94 (0.57–1.53)	0.95 (0.58–1.56)	25/384	2,811	0.99 (0.59–1.65)	0.99 (0.59–1.66)	0.96 (0.57–1.63)
4–6	35/415	2,948	1.20 (0.76–1.90)	1.24 (0.78–1.98)	1.27 (0.80–2.02)	42/439	3,198	1.43 (0.91–2.24)	1.34 (0.86–2.10)	1.32 (0.84–2.07)
≥7	39/517	3,883	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	35/514	3,788	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Test for trend[d]			0.99	0.98	0.97			0.71	0.76	0.83

[a]A total of 1,337 men undergoing radical prostatectomy at Johns Hopkins Hospital during 1993–2006. Follow-up began 1 year after prostatectomy.
[b]HR and 95% CI adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, and grade.
[c]HR and 95% CI adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, grade, smoking status, and mutually adjusted for BMI and physical activity.
[d]Median values of each category modeled in test for trend.

Table 3. Association of weight change from 5 years before to 1 year after prostatectomy with prostate cancer recurrence

	Weight change >2.2 kg			
	Median weight change (kg)	**Cases/total**	**Person years**	**HR (95% CI)[a]**
Decrease	−5.22	11/170	1,186	0.77 (0.38–1.53)
Maintenance	0	71/981	7,391	1.00 (Reference)
Increase	4.54	20/186	1,220	1.94 (1.14–3.32)
Test for trend[b]				0.02

[a]A total of 1,337 men undergoing radical prostatectomy at Johns Hopkins Hospital during 1993–2006. HR and 95% CI adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, grade, weight 5 years before prostatectomy, height, physical activity 1 year after prostatectomy, and smoking status.
[b]Median values of each category modeled in test for trend.

when the tumor is present, but not yet diagnosed, and cancer cells are escaping from the primary tumor before the prostatectomy. We thus addressed the influence of weight change on the ability of those cancer cells to escape, survive, and proliferate. Future studies should address whether weight change in the years following prostatectomy influences recurrence independent of weight change at diagnosis and surgery.

Although weight gain from young adulthood to middle age is not associated with or inversely associated with prostate cancer incidence in most (28–37), but not all, studies (38), only one previous study has addressed weight gain and prostate cancer recurrence. Strom and colleagues evaluated annual weight gain from age 25 to time of diagnosis; they reported an unadjusted 2-fold increased risk of recurrence among men with an annualized average weight gain more than 1.5 kg/y (8). Because only an unadjusted analysis was reported, it is unclear whether weight gain was a risk factor for recurrence independent of obesity and/or pathologic characteristics. In our study the positive association between weight gain and recurrence was independent of pathologic tumor characteristics as well as cigarette smoking status, physical activity level, weight, and height.

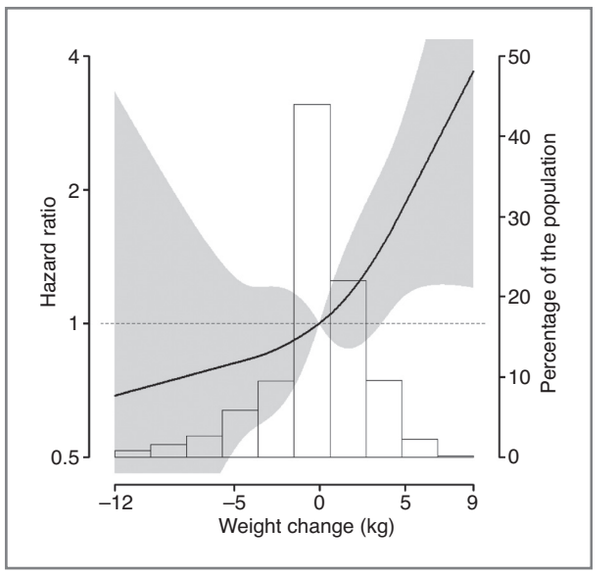

Figure 1. Multivariable-adjusted hazard ratio of prostate cancer recurrence associated with weight change by using restricted quadratic splines. Adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, grade, weight 5 years before prostatectomy, height, physical activity 1 year after prostatectomy, and smoking status. Gray shading represents 95% confidence interval; background histogram, distribution of weight change in study population.

In our study, obesity 1 year after surgery seemed to be associated with an increased risk of recurrence; an association that was attenuated among physically active men. Obesity in middle age has been extensively studied for prostate cancer incidence and mortality, and obesity at time of surgery for risk of prostate cancer recurrence. Specifically, obesity in middle age has been associated with a higher incidence of advanced stage and higher grade prostate cancer and a higher risk of death from prostate cancer, and obesity at diagnosis has been associated with higher case fatality in men with prostate cancer (22, 23). In contrast, obesity has been observed to be either not associated or inversely associated with risk of early-stage and low-grade disease (22, 23). Our findings for obesity at 1 year after surgery, although not statistically significant, are consistent with those from studies reporting a positive association between obesity at the time of surgery and recurrence (2–4, 7, 8, 12, 13, 15), including for a prior study conducted in prostate cancer patients of the one surgeon (5) and of multiple surgeons at Johns Hopkins Hospital (6).

We also evaluated whether the associations for weight change and obesity were modified by physical inactivity. We assessed these interactions because this potential modifiers; may also influence metabolic, hormonal, and inflammatory pathways (23, 39). Although we found suggestions that physical activity differentially influenced the associations of obesity and weight change with

Table 4. Association between BMI 1 year after prostatectomy and prostate cancer recurrence by physical activity level

BMI 1 year after prostatectomy (kg/m^2)	Cases/total	Person years	HR (95% CI)[a]	Weight change >2.2 kg	Cases/total	Person years	HR (95% CI)[b]
Physical activity <5 h/wk							
<25.0	12/176	1,286	1.00 (Reference)	Decrease	6/69	482	0.76 (0.27–2.11)
25.0—29.9	17/270	1,969	0.76 (0.35–1.65)	Maintenance	26/370	2,758	1.00 (Reference)
≥30.0	10/65	437	1.94 (0.76–4.93)	Increase	7/72	452	1.52 (0.57–4.06)
Test for trend[c]			0.12				0.42
Physical activity ≥5 h/wk							
<25.0	23/321	2,404	1.00 (Reference)	Decrease	5/101	704	0.68 (0.25–1.85)
25.0—29.9	33/451	3,297	0.85 (0.49–1.47)	Maintenance	45/611	4,633	1.00 (Reference)
≥30.0	7/54	404	1.11 (0.45–2.73)	Increase	13/114	768	2.10 (1.06–4.18)
Test for trend[c]			0.94				0.02

[a]A total of 1,337 men undergoing radical prostatectomy at Johns Hopkins Hospital during 1993–2006. HR and 95% CI adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, grade, smoking status, and physical activity 1 year after prostatectomy.
[b]HR and 95% CI adjusted for age, race/ethnicity, family history, year of prostatectomy, stage, grade, smoking status, physical activity 1 year after prostatectomy, weight at 5 years before prostatectomy and height.
[c]Median values of each category modeled in test for trend.

recurrence, these findings were not statistically significantly different.

We evaluated obesity, physical activity, and weight change in a cohort of men with prostate cancer who underwent radical prostatectomy performed by the same surgeon. Obesity is associated with worse stage/grade at the time of diagnosis (22, 23), which is, in turn, a strong predictor of recurrence. Thus, in our analysis, we adjusted for pathologic stage and grade, so that the independent effects of obesity and of weight gain could be detected. Because all men had to be healthy enough to undergo surgery, the prevalence of obesity was much lower in our sample than in the U.S. population. Despite this select group of patients of a single surgeon, we expect that our findings are generalizable across the range of BMI and weight change present in our study. Because these men had clinically localized disease, we had low power to perform subgroup analyses by stage and grade. Although obesity is associated with PSA in men without a diagnosis of prostate cancer, previous work found no difference in the performance of PSA as a predictor of biochemical recurrence by weight status (40). Adjustment for presurgery PSA level did not change our inferences. We asked the men to report their leisure time physical activity by using a single question; this measure was not validated and may not capture the full range of activity in all men. Our measures were retrospective, so may be subject to recall bias.

Obesity and weight gain in adulthood have been associated with numerous adverse health outcomes. Our study suggests that weight gain may also increase the risk of prostate cancer recurrence among men who have undergone radical prostatectomy to treat clinically localized prostate cancer. Thus, by avoiding weight gain, men with prostate cancer may both prevent recurrence and improve overall well-being.

Disclosure of Potential Conflicts of Interest

The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

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