A Diagnosis of Prostate Cancer and Pursuit of Active Surveillance Is Not Followed by Weight Loss: Potential for a Teachable Moment

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Abstract

Purpose—Obesity is a risk factor for incident prostate cancer (PC) as well as risk of disease progression and mortality. We hypothesized that men diagnosed with lower-risk PC and who elected active surveillance (AS) for their cancer management would likely initiate lifestyle changes that lead to weight loss.

Methods and Patients—Patients were enrolled in the Prostate Active Surveillance Study (PASS), a multicenter prospective biomarker discovery and validation study of men who have chosen AS for their prostate cancer. Data from 442 men diagnosed with PC within 1 year of study entry who completed a standard of care 12-month follow-up visit were analyzed. We examined the change in weight and body mass index (BMI) over the first year of study participation.

Results—After one year on AS, 7.5% (33/442) of patients had lost 5% or more of their on-study weight. The proportion of men who lost 5% or more weight was similar across categories of baseline BMI: normal/underweight (8%), overweight (6%) and obese (10%, Chi-Square test p=0.44). The results were similar for patients enrolled in the study one year or six months after diagnosis. By contrast, after one year, 7.7% (34/442) of patients had gained more than 5% of their weight.

Conclusion—Only 7.5% of men with low-risk PC enrolled in AS lost a modest (5%) amount of weight after diagnosis. Given that obesity is related to PC progression and mortality, targeted lifestyle interventions may be effective at this 'teachable moment', as men begin AS for low-risk PC.

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Introduction

Obesity has been associated with increased risk of prostate cancer (PC) progression among patients managed with active surveillance (AS).[1–6] Evidence from animal models suggests that weight loss may improve PC outcomes; however, this has not yet been demonstrated in human clinical trials.[7,8] In addition to a potential reduction in PC progression as well as other morbidities with weight loss, weight reduction may reduce the risk of treatment-related complications (e.g., urinary incontinence) in those men who ultimately require treatment in subsequent years due to disease progression.[3,9,10]

Many patients demonstrate remarkable lifestyle modifications after a diagnosis of low-risk prostate cancer.[11,12] These lifestyle changes include improved eating habits, increased daily physical activity, and weight loss. Few data exist on the effectiveness of these self-imposed lifestyle modifications that are done outside of formal programs. Population-based data suggest limited lifestyle modifications after diagnosis and potentially a reduction in exercise.[13,14]

A diagnosis of cancer is thought to represent a teachable moment for patients, at which time patients would be more likely to adopt healthy lifestyle changes resulting in weight loss. If these types of lifestyle changes are implemented, there may be an impact on cancer progression as well as a reduced risk of cardiovascular complications in the future.[15] We sought to investigate whether a new cancer diagnosis without specific discussion of lifestyle changes led changes in body mass index utilizing the Canary Prostate Active Surveillance Study (PASS), a large, multi-institutional, prospective study of men with localized prostate cancer on active surveillance.

Methods

PASS Study Population

Data are from the Canary Prostate Cancer Active Surveillance Study (PASS), a multicenter, prospective study (clinicaltrials.gov NCT00756665) of men who elected AS for PC management.[16,17] All men provided written informed consent prior to participation, and study procedures were approved by the local institutional review board for each study site. Men being seen in urology clinics were eligible for PASS if they had clinical stage T1-2 localized prostate cancer, no previous cancer treatment, no history of other malignancies (except non-melanoma skin cancer), an Eastern Cooperative Oncology Group (ECOG) status of 0 or 1, and were willing to participate in a structured AS protocol including quarterly PSA measures, semi-annual digital rectal examinations, and periodic surveillance prostate biopsies. There were no lifestyle or behavioral components as part of the protocol. The primary outcomes of PASS are the discovery and validation of biomarkers that predict outcomes to improve management of individual patients with prostate cancer.

Data Collection, Definitions, and Outcomes

At baseline, participants reported information on race/ethnicity, smoking status (never/former/current), alcohol use in the past year (one or more drinks per month), and family history of PC; clinic staff measured height and weight. Body mass index was calculated as

weight (kg) divided by height (m^2) and was categorized as normal (BMI < 25), overweight (25 BMI < 30), and obese (BMI 30).[18] The primary outcome of this analysis was percentage weight change, calculated as the difference in weight between baseline and year 1 visits divided by weight at baseline visit.

Statistical Analyses

Weight loss of 5% or more, a level endorsed by the U.S. Centers for Disease Control and Prevention for improving cardiovascular health (http://www.cdc.gov/healthyweight/ losing_weight/index.html), was of particular interest.[18] Weight maintenance was defined as change in weight of +/− 3% relative to baseline. Minimal weight change was defined as +/ −3.1%–4.9%, and modest weight change was defined as +/− 5%, an amount considered clinically meaningful. Weight change from baseline was compared across BMI categories using Fisher's exact tests. Multiple linear regression models were used to evaluate the association of percentage weight change with demographic characteristics, including age (<55 (reference), 55–64 and 65+ years), race (Caucasian (reference), African-American, Other), BMI (normal (reference), overweight, obese), smoking status (current/former vs. never (reference), alcohol intake (<1 drink/month (reference) vs. 1+ drink/month) and family history of PC (no (reference) vs. yes). Study site was considered as a random effect in linear mixed models, but was found to neither improve model fit nor markedly change the fixed effect estimates and therefore was not included in final models. Since the potential for weight change might be greatest among men with newly diagnosed PC, data and analyses are presented separately for the subset of men who enrolled in PASS within 12 months or within 6 months of their PC diagnosis date. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina). All statistical hypotheses were 2 sided, and $p < 0.05$ was considered statistically significant.

Results

Between September, 2008 and February, 2015, a total of 745 patients enrolled in PASS and had completed a 12-month follow-up visit. Of these men, 466 enrolled in PASS within one year, and 258 within 6 months, of PC diagnosis. Men enrolled later than 12-months from diagnosis or had missing data missing for any of the examined covariates were excluded, leaving 442 men for these analyses, 242 of whom were enrolled within 6 months of diagnosis. Demographic and health-related characteristics of study patients are displayed in Table 1. For the sample of patients enrolled within one year of cancer diagnosis, the mean age was 63 (SD=7), mean weight was 194 pounds (SD=32), and mean height was 70 inches (SD=3). Twenty-three percent (n=100) were normal, 52% (n=231) were overweight, and 25% (n=111) were obese. Overall, 7.5% (n=33) lost more 5% or more of their body weight after 1 year. The distribution of demographic characteristics among the subset of patients enrolled within 6 months of their diagnosis was similar to the overall study sample. While men with a BMI < 25 lost on average 0.1 pounds (SD=4.0), overweight and obese men gained 0.4 (SD=3.7) and 0.1 (SD=4.3) pounds, respectively, over the year after diagnosis.

Figure 1 shows the proportion of patients, for both the overall study sample and by BMI group, who lost, maintained, or gained weight during the first year of study enrollment after

PC diagnosis. In the overall sample of patients enrolled within one year of cancer diagnosis (Figure 1A) and the subset of patients enrolled within 6 months of cancer diagnosis (Figure 1B), the majority of men maintained their enrollment weight (65% and 61%changed weight by ±3% or less, respectively). Among the overall sample of patients enrolled within 12 months of PC diagnosis, similar proportions lost or gained more than 5% of their enrollment weight during the first year of study (7.5% and 7.7%, respectively; Figure 1A). A greater proportion of obese men had a weight loss of 5% compared to overweight or normal/underweight men (9.9% versus 6.1% and 8.0%, respectively), and a similar pattern was seen for weight gain of 5% (9.9% versus 8.2% and 4.0%, respectively), although the differences in weight gain 5% across baseline BMI categories was not statistically significant (Fisher's exact test p-value=0.24).

Among the subset of 242 patients who enrolled within 6 months of PC diagnosis, a slightly greater proportion of men lost or gained 5% of enrollment weight, compared to men who enrolled within 12 months of PC diagnosis (9.1% vs. 7.5% with modest loss and 9.1% vs. 7.7% with modest gain, respectively). In addition, the proportions of obese, overweight and normal/underweight men who lost 5% weight were slightly greater among the subset of patients enrolled within 6 vs. 12 months of diagnosis (12.9% vs. 9.9% for obese, 7.1% vs. 6.1% for overweight and 9.4% vs. 8.0% for normal weight, respectively).

Among the 442 patients who enrolled within 1 year of diagnosis, none of the baseline variables significantly predicted weight change (Table 2). In the subset of patients who enrolled within 6 months of diagnosis, men who had a family history of PC or did not regularly consume alcohol tended to lose more weight than men who did not have a family history of PC or were regular drinkers although these differences were neither clinically nor statistically significant (Table 2).

Discussion

In a sample of men with newly diagnosed, early stage PC enrolled in an AS study, of whom three-quarters were overweight or obese, we found little evidence to suggest that men made lifestyle changes that resulted in weight loss during the one-year period following enrollment in an AS study. The majority of men (286/442, 65%) maintained their enrollment weight (±3%), and only 7.5% of men lost 5% weight or more during the first year of AS. As troublesome, but perhaps not surprising, was the observation that a nearly equivalent number of men gained 5% or more from their enrollment weight (34/442, 7.7%) over the ensuing year.

These findings are consistent with those recently noted in a subset (n=511) of the Prostate testing for cancer and Treatment (PROTECT) trial in the United Kingdom in which no change in BMI after a diagnosis of PC was found.[19] No change in BMI was noted in this cohort despite approximately one-third of men modifying their behavior after their cancer diagnosis by reducing alcohol intake, quitting smoking, or increasing physical activity without deliberate intervention.[12,19] Men in the Prostate Cancer Prevention Trial (PCPT) overall only gained 1–2 1bs on average over the 7 years; however, the most at risk group for weight gain was men with low-grade cancer (71% higher annual weight gain than men with

no cancer, p=0.002).[20] This indicates men with a low grade prostate cancer diagnosis may actually be at risk for weight gain. Preliminary evidence suggests that small lifestyle modifications may make a difference in PC outcomes. For instance, in the Health Professionals Follow-up Study, a modest amount of vigorous activity for 3 hours a week was associated with lower overall and PC-specific mortality.[21]

A diagnosis of PC, even when 'low-risk', can be a psychologically-traumatizing event.[22] We sought to determine whether men make lifestyle changes that would result in weight loss. With the growing evidence that cancer-specific survival for men with low-risk PC on AS is remarkably high (98% or more), we further wondered if behavioral change and weight loss could contribute to these outcomes.[3,23]

The majority of men in this large prospective PC AS study had either not changed, or *increased*, their weight within one year after diagnosis. This striking observation supports the opportunity for a 'teachable moment' at the time of PC. Certainly, the simplest opportunity occurs if the patient decides to pursue a strategy of AS in which no other elements of his life change. However, weight loss and dietary changes surrounding other prostate cancer therapies may also be beneficial.[24]

There is no single best method to achieve weight loss; however, elements that are important for clinical success mentioned by the National Heart, Lung, and Blood Institute (NIH) include setting goals that are specific, doable, and forgiving.[25] They give an example of a goal that meets these requirements, such as "walk 30 minutes, 5 days each week" (https://www.nhlbi.nih.gov/health/educational/lose_wt/behavior.htm). This pointed information at the time of low-grade cancer diagnosis could be helpful to evoke behavioral change.

Men on AS for PC have a very low disease-specific mortality rate, and instead have a higher risk of death from competing causes. As a result, this moment is when the clinician can explain to the patient that lifestyle changes that reduce the risk of other causes of death (e.g., myocardial infarction, stroke, diabetes) would have a far-greater impact on health than interventions related to PC.[26,27, 25, 13] This study and the PROTECT trial show that overweight or obese men on AS are unlikely to modify their lifestyle and lose weight. Recently, the American Society of Clinical Oncology has established an initiative, which includes providing tools and resources for providers and patients regarding obesity including access to weight loss programs for cancer survivors.[28] Formal programs to provide support should be a component of follow-up plans for men on AS.

Only 7.5% of men embarking in a program of active surveillance for low-risk prostate cancer had a modest amount of weight loss of at least 5% reduction from baseline weight. Physician facilitated multi-disciplinary weight loss programs for all patients on surveillance for prostate cancer should be further investigated.

Acknowledgments

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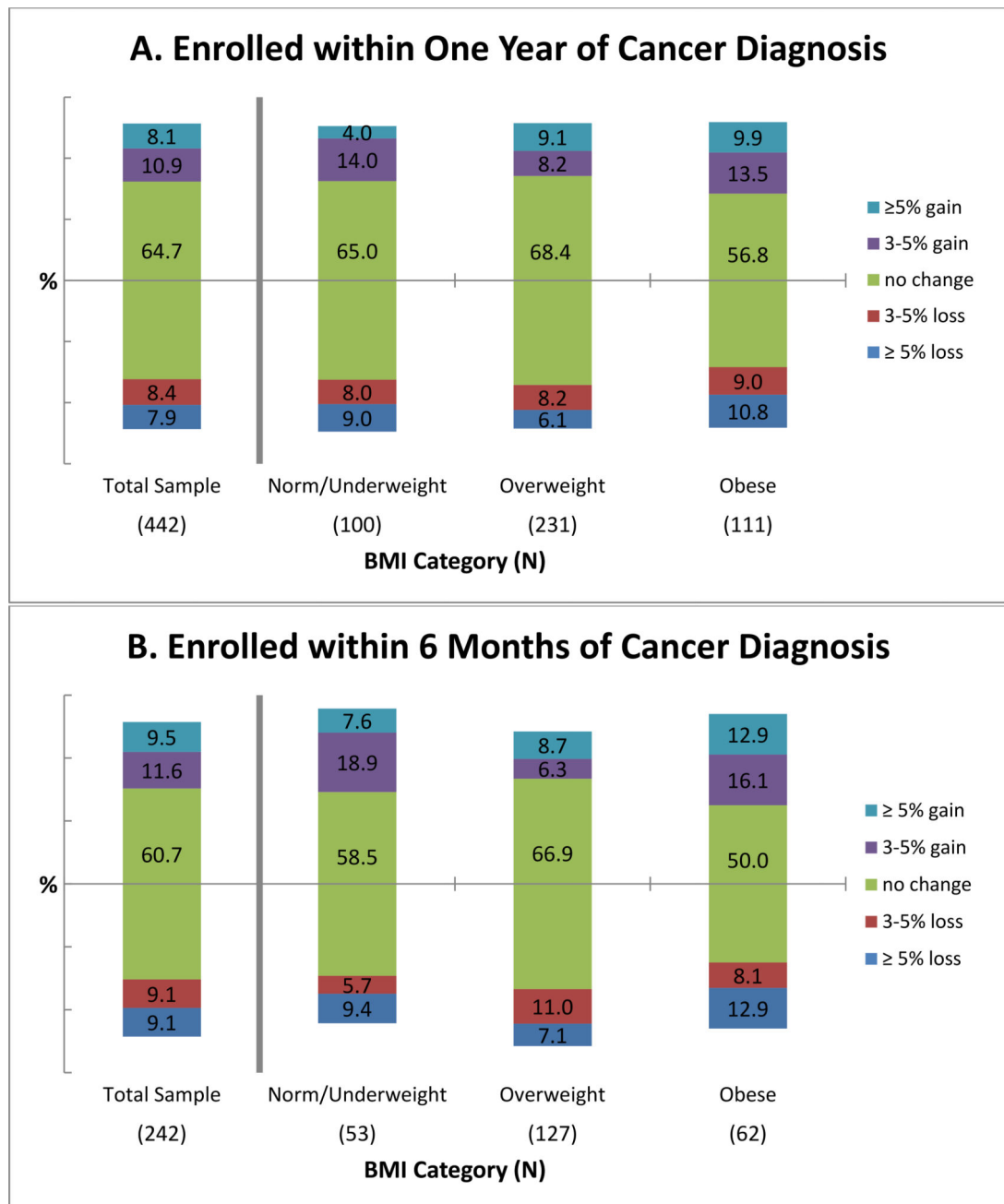
Figure 1.
Change in weight during first year of enrolment in an active surveillance protocol. Results are shown for the total cohort and by BMI category, both for all participants enrolled in the study within one year of cancer diagnosis **(A)** and for those enrolled within 6 months of cancer diagnosis **(B)**.

Table 1

Demographics of the study cohort

Results are shown for all participants diagnosed with prostate cancer within 1 year before study enrollment and a subset of those diagnosed within 6 months before enrollment.

Demographics	Diagnosed within 1 year of enrollment N(%) or mean (SD)	Diagnosed within 6 months of enrollment N(%) or mean (SD)
	N=442	N=242
Age (years)	63 (7)	634 (7)
< 55	57 (13)	22 (9)
55 ≤ Age < 65	182 (41)	106 (44)
≥ 65	203 (46)	114 (47)
Race		
Caucasian American	384 (87)	206 (85)
Hispanic/Latino	20 (5)	12 (5)
African American	19 (4)	10 (4)
Asian	12 (3)	9 (4)
Other	7 (1)	5 (2)
Weight, baseline (pounds)	194 (32)	195 (32)
Height, baseline (inches)	70 (3)	70 (3)
Body Mass Index (kg/m^2)		
<25	100 (23)	53 (22)
25 ≤ BMI < 30	231 (52)	127 (52)
≥ 30	111 (25)	62 (26)
Lost 5% Body Weight	33 (7)	22 (9)
Cigarette Use		
Current	17 (4)	7 (3)
Former	172 (39)	101 (42)
Never	253 (57)	134 (55)
Alcohol Use (in past 12 mo.)		
Yes	370 (84)	198 (82)
No	72 (16)	44 (18)
Family History of PCa		
Yes	111 (25)	65 (27)
No	331 (75)	177 (73)

Table 2

Association between weight change and patient characteristics

Weight change is recorded as Least Square (LS) means and standard errors (SE) from linear regression model.

Baseline Demographics	Diagnosed within 1 Year of enrollment (N = 442)			Diagnosed within 6 Months of enrollment (N = 242)		
	Mean Baseline Weight (lb)	Weight change (lb) from baseline to year 1	P-value*	Mean Baseline Weight (lb)	Weight change (lb) from baseline to year 1	P-value*
Age						
<55	194	0.26 (0.63)		190	−0.19 (1.02)	
55 Age < 65	200	0.26 (0.48)	0.59	200	−0.53 (0.72)	0.94
65	189	−0.13 (0.46)		191	−0.53 (0.67)	
Race						
African American	197	0.62 (0.91)		202	−0.37 (1.39)	
Caucasian	194	−0.19 (0.31)	0.67	195	−0.32 (0.47)	0.97
Other	192	−0.04 (0.67)		194	−0.55 (0.92)	
Body Mass Index						
Under / Normal	162	−0.40 (0.61)		162	−0.90 (0.90)	
Overweight	190	0.33 (0.49)	0.40	191	−0.75 (0.74)	0.41
Obese	232	0.46 (0.61)		232	0.41 (0.90)	
Smoking Status						
Current / Former	197	0.29 (0.48)		199	−0.08 (0.73)	
Never	192	−0.04 (0.45)	0.40	192	−0.74 (0.65)	0.24
Alcohol intake (prior year)						
1+ drink per month	196	0.47 (0.40)		197	0.21 (0.60)	
<1 per month	188	−0.21 (0.57)	0.18	186	−1.03 (0.84)	0.09
Family history of PCa						

Baseline Demographics	Diagnosed within 1 Year of enrollment (N = 442)			Diagnosed within 6 Months of enrollment (N = 242)		
	Mean Baseline Weight (lb)	Weight change (lb) from baseline to year 1	P-value*	Mean Baseline Weight (lb)	Weight change (lb) from baseline to year 1	P-value*
Yes	198	−0.07 (0.50)	0.36	198	−0.88 (0.76)	0.13
No	193	0.33 (0.45)		194	0.05 (0.65)	

*
P-value from Type 3 Test, which tests the significance of each variable in the model, given all other variables in the model. Regression models are adjusted for baseline weight.