Adoption of a Plant-Based Diet by Patients with Recurrent Prostate Cancer

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The Western diet has been associated with prostate cancer incidence as well as risk of disease progression after treatment. Conversely, plant-based diets have been associated with decreased risks. A pilot clinical trial of a 6-month dietary change and stress reduction intervention for asymptomatic, hormonally untreated patients experiencing a consistently rising PSA level, the first sign of recurrence of prostate cancer after surgery or radiation therapy, was conducted to investigate the level of intake of plant-based foods and the relationship between intake and the change in the rate of PSA rise. A pre-post design was employed in which each patient served as his own control. In this multifaceted intervention, patients and their spouses were encouraged to adopt and maintain a plant-based diet. The prestudy rate of PSA rise (from the time of posttreatment recurrence to the start of the study) was ascertained by review of patients' medical records. Dietary assessments were performed and prostate-specific antigen (PSA) levels ascertained at baseline, prior to the start of intervention, and at 3 and 6 months. Changes in numbers of servings of plant-based food groups were calculated and compared with rates of PSA rise over the corresponding time intervals. Median intake of whole grains increased from 1.7 servings/d at baseline to 6.9 and 5.0 servings/d at 3 and 6 months, respectively. Median intake of vegetables increased from 2.8 servings/d at baseline to 5.0 and 4.8 servings/d at 3 and 6 months, respectively. The rate of PSA rise decreased when comparing the prestudy period (0.059) to the period from 0 to 3 months (–0.002, $P < .01$) and increased slightly, though not significantly, when comparing the period from 0 to 3 months to the period from 3 to 6 months (0.029, $P = .4316$). These results provide preliminary evidence that adoption of a plant-based diet is possible to achieve as well as to maintain for several months in patients with recurrent prostate cancer. Changes in the rate of rise in PSA, an indicator of disease progression, were in the opposite direction as changes in the intake of plant-based food groups, raising the provocative possibility that PSA may have inversely tracked intake of these foods and suggesting that adoption of a plant-based diet may have therapeutic potential in the management of this condition.

Keywords: *prostate; prostatic neoplasms; prostate-specific antigen; rising PSA; PSA doubling time; plant-based diet; stress reduction; complementary and alternative medicine; disease progression*

Carcinoma of the prostate is the most commonly occurring cancer (other than skin cancer) among men in Western populations. In the United States, 1 man in 6 will develop prostate cancer in his lifetime.[1] Most patients who present with prostate cancer receive definitive primary treatment consisting of either surgical removal of the prostate (radical prostatectomy [RP]), radiation therapy to the prostate (RT), or surgical removal followed by radiation to the prostatic bed or pelvis. Despite treatment, about one third of patients will have a biochemically defined recurrence, marked by successive increases in prostate-specific antigen (PSA) levels after a posttreatment nadir (the lowest PSA value observed after RP or RT), within the first 10 years.[2] These individuals are at increased risk of metastasis formation and premature death; more than a third of those with rising PSA will go on to develop metastatic disease within the subsequent 5 years.[2]

In those who have undergone a recurrence, PSA typically tends to rise exponentially after prostatectomy or radiation therapy, reflecting the gradual, inexorable growth of the cancer in the body.[2-4] After local treatment, the rate of PSA rise is the single best predictor of both the probability of and time to development of overt metastatic disease,[2,3] as well as of overall survival.[5,6] Hormonal therapy is sometimes employed at this point, although there is little evidence that early use significantly improves prognosis except in the subset of patients with pelvic lymph

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node metastasis. Hormonal therapy also frequently produces side effects including hot flashes, loss of libido, gynecomastia, and loss of bone and muscle mass. Therefore, many physicians employ a strategy of active surveillance.[7,8] Yet patients, keenly aware of the paucity of curative treatment options, frequently suffer from severe anxiety as they watch their PSA levels continue to rise. This has motivated a search for novel adjunctive strategies that could retard tumor progression while avoiding the side effects of hormonal therapy.

In searching for new therapeutic options, it is important to begin by examining the possible underlying causes of prostate cancer. Dramatic international variations in age-adjusted incidence and mortality rates provide clues to the etiology of prostate cancer. For example, Qidong County in China has an incidence rate of only 0.8 per 100 000 men, whereas the rate for African American men in Atlanta is 102.1 per 100 000, a relative risk of 127.5.[9,10] Some of these differences may be accounted for by the much higher level of PSA screening and detection in the United States compared with China. Yet Japanese men, like Chinese, also have much lower incidence and mortality rates than Americans do. The large difference in rates between the United States and Japan has been observed for decades, long before the advent of PSA testing. Upon migration to the United States, prostate cancer rates in Japanese men increase 4- to 9-fold within the first generation and approximate US rates by the second generation.[11-13]

While this does not rule out the possibility that genetic polymorphisms (naturally occurring or induced variation in the sequence of genetic information on segments of DNA) may sometimes be part of the causal chain, it does suggest that the disease is driven more by some form of environmental or lifestyle exposures than by genetic factors.[14] Japan is a densely populated, heavily industrialized country whose population, perhaps even more than that of the United States, is exposed regularly to many potential carcinogens. This suggests that pollution is not the critical factor in explaining higher prostate cancer incidence in the United States. Numerous studies, therefore, have focused on lifestyle factors (smoking, physical activity, sexual history, occupation, diet) and patterns in search of the explanation for the differences in incidence rates. With the exception of diet, most lifestyle factors have not been associated with prostate cancer incidence.[15-24]

Epidemiologic and laboratory investigations suggest that diet may constitute an important set of environmental factors affecting development and progression of prostate cancer. As reviewed by Kolonel and colleagues, 16 of 22 studies (14 case control and 8 cohort) found a positive association of meat intake with prostate cancer risk, with 15 showing odds ratios or relative risks of 1.3 or more.[25] Similarly, in a review by Chan et al, 12 of 23 studies (14 case control and 9 cohort) found positive associations of dairy foods with prostate cancer risk.[26] Arachidonic acid, synthesized endogenously from omega-6 fatty acids and also found preformed (in cell membranes) in foods of animal origin, has been shown to stimulate the growth of both LNCaP (hormone-sensitive) and PC3 (hormone-insensitive) cell lines and is as effective as testosterone in stimulating growth of LNCaP cells.[27]

Conversely, plant foods including whole grains, vegetables, legumes, and fruits, appear to be protective. As summarized in a recent review by Chan and colleagues, 8 of 16 studies (13 case control and 3 cohort) reported an inverse association of specific or total vegetable intake with prostate cancer risk, whereas 8 reported no association. None reported increased risk. The strongest protective effects were seen for beans and legumes, nuts, carrots, leafy greens, cruciferous vegetables (cabbage family), and tomatoes.[28] Cruciferous vegetables have been found in 2 population-based studies to be associated with a reduction in prostate cancer incidence.[29,30] Indole-3-carbinol, derived from diets rich in cruciferous vegetables, inhibits the growth of PC3 human prostate cancer cells by inducing G1 cell cycle arrest leading to apoptosis and regulates the expression of apoptosis-related genes.[25] In addition, cruciferous vegetables are rich sources of the isothiocyanate sulforaphane. Sulforaphane has been shown to upregulate phase 2 enzymes in a variety of human prostate cancer cell lines, an induction that appears to be mediated by increased transcription of the NQ0-1 gene.[30]

Growing evidence further suggests that dietary modification emphasizing, in particular, increased whole grain and vegetable intake (as stressed in macrobiotic and many vegan diets) may influence the course of prostate cancer after diagnosis. Adoption of whole grain– and vegetable-based macrobiotic and vegan diets has been associated with prolonged survival and documented remissions of bone and visceral metastases in men with advanced prostate cancer.[31] Plant-based diet intervention trials were found to significantly reduce the rate of PSA rise in patients with recurrent disease[32] and to lower overall PSA, in comparison with randomized controls, in patients with untreated disease.[33]

In the University of California, San Diego (UCSD), Healthy Men Study, a pilot clinical trial of a plant-based diet reinforced by stress reduction, we examined the effect of the intervention on disease progression in patients with recurrent prostate cancer. The dietary changes that were promoted in this intervention were far reaching. Even under the simplest of circumstances,

dietary intervention is a challenging task that involves both the initiation and maintenance of the desired change. It is made even more complex when the goal is the restructuring of an entire dietary pattern, as was the case in this intervention. In this article, we therefore focus on the dietary aspects of the intervention. We measure the extent to which patients adopted the recommended diet by assessing changes in the daily servings of specified food groups, particularly whole grains and vegetables. In addition, we explore the relationship between the change in intake of these food groups and the change in the rate of the rise in PSA, a marker of the rate of prostate cancer progression.

Patients and Methods

Study Design

The UCSD Healthy Men Study was a pre-post pilot clinical trial in which each patient served as his own control. Its purpose was to determine whether a plant-based dietary intervention, reinforced by stress reduction, could effect a major dietary change and influence the progression of recurrent prostate cancer. In this article, we examine the level of intake of the intervention diet by patients at each of the 3 study time points—baseline, 3 months, and 6 months—and we explore whether the changes in the rates of PSA rise from 0 to 3 months and 3 to 6 months track changes in dietary intakes during the corresponding intervals.

Patients

Fourteen study-eligible patients were recruited with the assistance of urologists at the UCSD and San Diego Veterans Affairs Medical Centers and community hospitals. All patients provided informed consent before being enrolled in the study. Patients were eligible if they had biopsy-confirmed, operable, invasive prostate cancer that was treated by radical prostatectomy or radiation therapy; had rising PSA documented on a minimum of 3 serial tests, each at least 1 month apart from the others, after achieving posttreatment nadir; had no radiological or pathological evidence of overt metastatic disease since completion of initial local treatment; and had not used any form of hormonal therapy for at least 12 months prior to the last nadir PSA.

Intervention

Patients participated, along with their spouses or another designated support person, in an intensive 6-month individual- and group-based diet and stress reduction intervention conducted at the Moores UCSD Cancer Center. They were taught to increase intake of whole grains, vegetables, fruit, and legumes and to decrease meat, dairy, and refined carbohydrates. The intervention used a baseline orientation and individual dietary counseling, instructional materials, ongoing weekly (and, later, monthly) group meetings that included a cooking class and shared model meal, and individual telephone follow-up counseling. The emphasis was placed on increasing intake of the plant-based foods rather than on strict avoidance of meat, dairy, and refined carbohydrates. It was anticipated that by focusing on what to consume rather than on what to avoid, the plant-based foods would gradually displace the foods to be minimized while engendering less resistance to the overall change. Among the plant-based food groups, the primary focus was placed on increasing consumption of the staples, whole grains and vegetables, with a secondary focus on fruit and legumes. Patients were encouraged to eat a combined volume of these foods sufficient to provide approximately 1600 kcal/d. This pattern, as well as appropriate portion sizes, were modeled in the shared meals. Patients were instructed by the dietitian to modify serving sizes as needed to take account of differences in energy requirements.

The intervention included a series of 10 three-hour group meetings over the 6-month period (once per week during the first month, once per month during months 2 to 5, and twice during month 6). At most meetings, patients and spouses/support persons received a hands-on cooking demonstration, were served a healthy meal, and participated in supportive group discussion. During the group meetings, patients were also taught how to practice meditation as well as how to perform several basic yoga and t'ai chi movements. They were also encouraged to engage in a daily practice of 1 or more of these disciplines. Group meetings were more frequent initially to assist patients to initiate and adopt the diet and stress reduction changes during the initial transition period. They were less frequent afterward because their role was to support and maintain changes that had already been made.

Patients also received telephone calls from the dietitian on a weekly basis throughout the intervention. During these calls, patients were guided in dietary goal setting, problem solving, and self-monitoring and counseled regarding any specific questions or concerns that had arisen.

Measurements

Data Collection, Assessments, and Phlebotomy

Data collection and assessments, as well as phlebotomy, were performed primarily at the UCSD General Clinical Research Center ambulatory clinic. Medical records were collected and reviewed prior to

baseline to confirm study eligibility and to obtain prestudy PSA and treatment histories, tumor characteristics, and other clinical information. Demographic and identifying data were collected at baseline only. Assessments of diet, anthropometric status, physical activity, practice of stress reduction, symptoms, and disease-related quality of life were performed at each study time point. Phlebotomy was also performed at baseline and 3 and 6 months and was used for determination of study-period PSA levels.

Dietary Assessment

Diets were assessed using 24-hour recall to ascertain the degree of adoption of the plant-based diet. A 24-hour recall was administered in person by a nutritionist at clinic visits at each of the study time points: baseline, 3 months, and 6 months. Additional 24-hour recalls were performed over the telephone within 3 weeks of the 3-month time point (for an average of 3.2 recalls) and 6-month time point (for an average of 2.6 recalls). However, only one 24-hour recall could be used at baseline (the one that preceded the baseline study orientation) because several patients began implementing dietary changes immediately after the orientation but before completing all of their additional baseline dietary assessments. The additional 24-hour recalls were ultimately not used because (1) they were performed by telephone, not in person; (2) they were not conducted on the same date as phlebotomy (but rather were performed as much as 3 weeks before or after the clinic visits); and (3) the number of these assessments varied by subject.

The dietitian used the US Department of Agriculture multipass interview method to probe food consumption on the previous day, a procedure that is well established and has been described and validated previously.[34,35] Raw data from these interviews were processed for food group and nutrient analysis using the Nutrition Data System (NDS-R 2005, University of Minnesota, Minneapolis) software and the University of Minnesota (Minneapolis) database.

After processing the raw data, several categories of NDS output data were combined to create each of the food groups used in the present analysis. The whole grain food group was coded to include only whole kernel grains or 100% whole grain products; it did not include partial whole grain products such as whole grain crackers and chips in which the whole grain content was <100%. The vegetable food group included dark green vegetables, tomatoes, vegetable juice, and "all other vegetables"; it did not include white potatoes or fried vegetables (to exclude highly processed foods such as french fries). The legume food group included cooked dried beans and soy foods. The fruit food group included citrus as well as noncitrus fruit but not fruit juice (to exclude juices that had added sugar).

Serving sizes varied depending on the specific food and whether it was cooked or raw. For whole grains and legumes, 1 serving was equal to ½ cup cooked. For vegetables as well as fruit, 1 serving was equal to 1 cup if raw or ½ cup if cooked.

Determination of Absolute PSA and Rate of PSA Rise

Prestudy PSA readings were obtained by reviewing patients' medical records. The rate of PSA rise for the period prior to intervention (covering the period from the end of the posttreatment PSA nadir up to, but not including, baseline) was derived from prestudy PSA readings. The complete methodology used to ascertain prestudy PSA readings is described elsewhere.[36] Linear regression modeling of the natural logarithm of PSA was used to calculate rates of PSA rise for each patient for the following periods: prestudy, 0 to 3 months, and 3 to 6 months.

The rates of PSA rise at 3 months (reflecting the change in PSA from 0 to 3 months) and 6 months (reflecting the change in PSA from 3 to 6 months) were derived from PSA readings (1 reading obtained for each time point) that were performed at the main UCSD Medical Center Chemistry Lab on serum samples obtained at each time point. Intervention period PSA tests were performed using the Immulite 2000 PSA test kit (Diagnostic Products Corp, Los Angeles, Calif), a completely automated, ultrasensitive chemiluminescence assay with a sensitivity limit of 0.04 ng/mL.

Data Analysis

Descriptive statistics were calculated for patient characteristics at baseline, dietary intakes of plant-based food groups (at baseline, 3 months, and 6 months), and the rate of PSA rise (prestudy, 0-3 months, and 3-6 months). The rates of PSA rise were compared, using the Wilcoxon signed-rank test for paired data, for the following periods: Prestudy versus 0 to 3 months; 0 to 3 months versus 3 to 6 months. Comparisons were conducted at the $\alpha = .05$ level of significance. All analyses were conducted using SAS (version 8.01; SAS Institute Inc, Cary, NC, 2000).

Results

Study Participants

Fourteen recurrent prostate cancer patients were enrolled; 1 elderly patient withdrew from the study prior to his baseline visit, so his baseline data were not available. Table 1 shows the baseline characteristics

Table 1. Baseline Characteristics of Each Patient Enrolled

Patient Number	*Age, y*	*Race/Ethnicity*	*Marital Status*	*BMI, kg/m²*
1	74	Hispanic	Married	33.16
2	72	Non-Hispanic White	Married	23.97
3	63	Non-Hispanic White	Married	23.91
4	77	Non-Hispanic White	Married	24.64
5	63	Non-Hispanic White	Married	22.33
6	64	Non-Hispanic White	Married	30.56
7	70	Non-Hispanic White	Single	25.49
8	83	Non-Hispanic White	Married	22.86
9	—	—	—	—
10	52	Non-Hispanic White	Married	25.91
11	56	African American	Married	37.73
12	74	Non-Hispanic White	Married	23.34
13	82	Non-Hispanic White	Married	27.77
14	57	Non-Hispanic White	Single	25.15

BMI = body mass index. Patient 9 withdrew at baseline; therefore, demographic data were not available.

for the remaining 13 patients who participated in the study. Study participants were predominantly non-Hispanic White (85%), older (median age = 70 years), married (85%), and overweight (54% with BMI ≥25; Table 1).

Only 10 of the 13 patients were evaluable by the end of the study; patients 10 and 14 reported using hormone therapy almost immediately after starting the intervention. They were both younger men who were extremely anxious about their rising prestudy PSA levels, had been debating whether to use hormonal therapy prior to enrollment, and were uncomfortable relying solely on diet. Both, supported by their urologists, made the decision to initiate hormonal therapy within the first month of the intervention, before making substantive dietary changes; their decisions to use hormonal therapy were unrelated to the efficacy of the intervention. Patient 11, also a younger man, withdrew prior to his 6-month visit. He found the dietary changes onerous and may have lacked spousal support. However, his PSA level was stable during the first 3 months of the intervention. The remaining 10 patients were included in the subsequent analyses.

Whole Grain and Vegetable Consumption

Table 2 shows the median intake of plant-based food groups and their subgroups at baseline, 3 months, and 6 months. The results focus primarily on the intake of whole grains and vegetables since these 2 food groups were given emphasis during the intervention.

At baseline, the median intake of whole grains was 1.7 servings/d. The median servings per day of whole grains significantly increased from baseline to 6.9 and 5.0 servings/d at 3 and 6 months, respectively ($P < .01$ for both comparisons) indicating a 306% increase after 3 months and a 194% increase after 6 months.

At baseline, the median intake of vegetables was 2.8 servings/d. The median servings per day of vegetables increased from baseline to 5.0 and 4.8 servings/d at 3 and 6 months, respectively, indicating a 79% increase after 3 months and a 71% increase after 6 months.

Before the intervention, only 20% of the study participants were consuming 3 or more servings per day of whole grains, and 40% were consuming 3 or more servings per day of vegetables, but after 6 months, 80% of the patients achieved this level of intake for whole grains and 60% for vegetables.

Figure 1 shows the median intake of total whole grains and total vegetables at baseline, 3 months, and 6 months. The median servings per day for both whole grains and vegetables peaked at 3 months and then decreased slightly at 6 months. However, the total median intake for both remained approximately 5 servings/d at 6 months.

Rate of PSA Rise

Figure 2 shows the rates of PSA rise for prestudy, 0 to 3 months, and 3 to 6 months. Individual-level data on patients' rates of PSA rise are provided elsewhere.[36] The median (range) rate of PSA rise for prestudy was 0.059 (0.014 to 0.129). From 0 to 3 months, the median (range) rate of PSA rise was –0.002 (–0.096 to 0.079), representing a significant decrease from the rate during the prestudy period ($P < .01$). The negative value indicates a median reduction in absolute PSA. From 3 to 6 months, the median (range) rate of PSA rise was 0.029 (–0.067 to 0.136),

Table 2. Median Intake of Plant-Based Food Groups

	Servings per Day					
	Baseline		*3 Mo*		*6 Mo*	
Food Group	*Median*	*Range*	*Median*	*Range*	*Median*	*Range*
Whole grains[a]						
Total whole grains	1.7	0.0-5.1	6.9	0.0-11.9	5.0	1.1-8.1
> 3 servings/d whole grains, n (%)	2 (20.0)	6 (60.0)	8 (80.0)			
Vegetables[b]						
Dark greens	0.0	0.0-5.0	1.3	0.0-3.8	0.4	0.0-3.0
Tomatoes	0.7	0.0-2.6	1.3	0.0-3.1	1.1	0.0-4.3
Other vegetables	1.0	0.0-7.8	2.0	0.6-13.0	1.8	0.3-8.6
Vegetable juice	0.0	0.0-7.5	0.0	0.0-0.5	0.0	0.0-2.5
Total vegetables and juice	2.8	0.2-20.9	5.0	0.6-15.6	4.8	1.8-12.4
> 3 servings/d vegetable, n (%)	4 (40.0)	9 (90.0)	6 (60.0)			
Fruit[c]						
Citrus	0.0	0.0-2.8	0.0	0.0-0.1	0.0	0.0-0.8
Other fruit	1.7	0.0-4.0	3.3	1.0-4.6	2.3	1.0-8.0
Total fruit	2.0	0.0-6.8	3.3	1.0-4.6	2.3	1.0-8.3
> 2 servings/d fruit, n (%)	5 (50.0)	8 (80.0)	6 (60.0)			
Beans and legumes						
Cooked dry beans	0.0	0.0-1.0	0.5	0.0-2.1	0.0	0.0-2.6
Soy foods (eg, tofu, miso)	—	—	0.2	0.0-3.6	0.0	0.0-1.0
Total beans and legumes	0.0	0.0-1.0	1.1	0.0-3.6	0.5	0.0-2.6
> 2 servings/d beans and legumes, n (%)	0 (00.0)	3 (30.0)	2 (20.0)			

From the Healthy Men Study 24-hour recall data (N = 10).
a. Only 100% whole grain; does not include partially whole grain. Healthy People 2010 goal is ≥3 servings/d.
b. Does not include white potatoes. Healthy People 2010 goal is ≥3 servings/d.
c. Does not include fruit juice. Healthy People 2010 goal is ≥2 servings/d.

representing a nonsignificant increase when compared to the 0- to 3-month period ($P = .4316$).

Discussion

Our study investigated 2 related issues. First, we examined the degree to which patients with recurrent prostate cancer, enrolled in an intensive diet and stress reduction intervention, changed their intake of plant-based foods. We specifically focused on the change in the level of intake of the 2 staple food groups of a plant-based diet, whole grains and vegetables. We also examined the change in intake in secondary food groups—legumes and fruit—as well as in selected subcategories of special interest within the larger groups. Second, we explored whether the observed changes in dietary intake tracked changes observed in the rate of PSA rise, a marker of disease progression in recurrent prostate cancer.

The intervention resulted in a large, statistically significant increase in intake of whole grains from baseline levels; intake had more than quadrupled by 3 months and was still nearly triple baseline levels at 6 months. Vegetable intake also increased from baseline, though not as dramatically. Intake of other plant-based food groups also increased from baseline, as did intake of most selected subgroups. For example, the median intake of dark green vegetables, rich in lutein, indothiocyanate, insoluble fiber, and other compounds with possible anticancer activity, increased from 0 at baseline to 1.3 servings at 3 months but dropped back to 0.4 servings by 6 months.

We also found that as the rate of rise in PSA, a marker of disease progression, decreased, the intake of both whole grains and vegetable increased, raising the interesting possibility that PSA may have tracked the intake of these foods. Thus, during the first 3 months of the intervention, when the intake of both whole grains and vegetables increased substantially, the median rate of PSA rise not only declined but became negative, reflecting a slight median reduction in absolute PSA and possible disease regression, at least in a few of the 5 patients with absolute reductions. Conversely, during the second 3 months of the intervention, when whole grain intake decreased moderately and vegetable intake declined slightly from their levels at 3 months, the PSA began rising again, although more slowly than during the period prior to baseline.

What are the implications of these observations? First, they suggest that under the right circumstances, it is possible to effect substantial short-term changes in

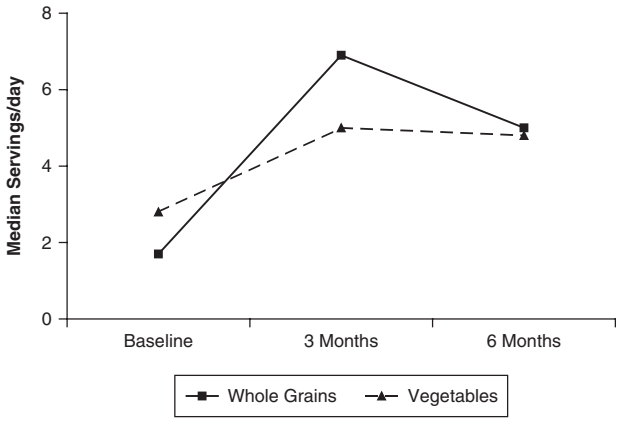

Figure 1 Servings per day of whole grains and vegetables.

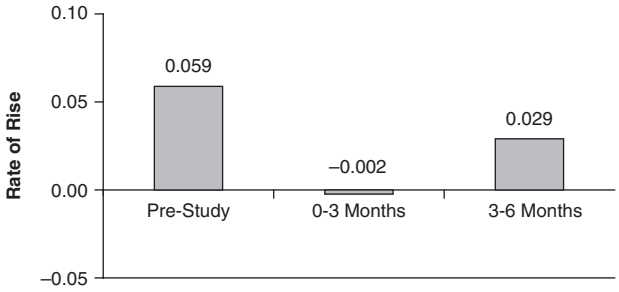

Figure 2 Median rate of prostate-specific antigen rise.

the direction of a plant-based dietary pattern. While this type of pattern would need to be maintained for the long term by patients for it to have lasting clinical value, this is a necessary first step. We did observe some recidivism by 6 months, underscoring the common wisdom that long-term maintenance of healthy dietary change is not easy. Furthermore, we did not follow patients past 6 months, so we have no estimate of how enduring these changes would be over a longer period, particularly without the coaching and support offered by the intervention. However, in the Prostate Cancer Lifestyle Trial,[37] prostate cancer patients who were randomized to the intervention arm reported a high level of adherence at 12 months to a vegan, plant-based dietary pattern similar to that employed in our study. Still, documentation of continued adherence for an even longer period would be desirable.

The dietary changes made by patients may have resulted from a number of factors, some intrinsic to this particular study population and others to the nature of the intervention. Patients with recurrent prostate cancer may be especially motivated to make such changes. This is no doubt due in part to their keen awareness of the paucity of curative or even life-extending therapeutic options and their knowledge of the side effect profile of the one line of available treatment, hormonal therapy. At the same time, there is usually a window of time, ranging from a number of months to many years, during which they will likely remain asymptomatic and have the ability to effect dietary changes free from the distraction or demoralizing effects of symptomatic metastatic disease. Further motivation may be afforded by the knowledge that the same dietary changes may protect against comorbidities (eg, diabetes, hypertension, arthritis) commonly seen in older men and from which they might be suffering.

In addition to these intrinsic motivational factors, the intervention employed several strategies to foster the desired dietary changes. First, involvement of the spouses (or another designated support person) was strongly encouraged. Wives or partners attended most group meetings as well as many clinic appointments and provided a "fifth column" that could be drawn on to provide support to patients. Group meetings (which included hands-on cooking classes, group-based stress management training, and shared meals) may have been important in promoting dietary change. Interestingly, the frequency of classes was much greater during months 0 to 3, when the intake of plant-based food groups was highest, than during months 3 to 6, when the intake of plant-based foods declined somewhat. Individual dietary counseling at baseline and follow-up telephone counseling throughout may have helped to further orient patients to the diet and to problem solve any resistance or situational obstacles encountered. Further study is needed to examine the relative importance of these supportive factors.

Our findings perhaps suggest that prostate cancer could respond to changes in diet, even over a relatively short period of time. The potential sensitivity of prostate cancer to such short-term changes is of great biological and clinical significance and will need to be closely examined in future studies. Biologically, it could indicate that diet may play a large role in prostate cancer progression and would be consistent with the proposition by Amling[38] that body weight, while not associated with prostate cancer incidence, appears to be a key factor driving progression. Most patients lose weight on a plant-based diet, as was observed in an earlier study by Saxe et al,[32] and weight reduction may turn out to be an important factor mediating the effect of a plant-based diet on progression, a possibility that we plan to explore. Clinically, the possibility that changes in rates of PSA rise might track changes in diet would also be significant. Taken together with another finding from this study reported elsewhere[36] that there was a significant decrease from prestudy in the rate of PSA rise over the entire 6-month study period, it would suggest that dietary modification

may provide a new therapeutic option for recurrent prostate cancer.

While our study raises the possibility that the change in the rate of PSA rise tracked changes in dietary intake of plant-based food groups, larger randomized trials, using the most rigorous and reliable possible measures of self-reported dietary intake and validated by more objective measures such as plasma carotenoids and anthropometry, will be needed to properly test this concept. One question that might warrant investigation in such a study is whether a dose-response relationship exists between adherence and the degree of disease control. Another is how to best assist clinicians to support and guide their patients in structured, monitored dietary modification.

It should be noted that a variety of factors other than the change in intake of plant-based food groups could have accounted for the change in the rate of PSA rise, such as a concomitant reduction in another food group (eg, red meat, dairy, refined carbohydrates) that was displaced in the diets of patients, changes in body weight or energy expenditure, or stress management training–induced modulation of patients' sympathetic tone (which, in turn, could have led to immune modulation or reductions in circulating levels of proinflammatory, possibly tumor-promoting, intermediates). In addition, the reduction in the rate of rise in PSA may have been artifactual, resulting from "noise" or variability in the PSA test itself. Still, if changes in the dietary pattern indeed affected the direction of disease progression and did so in such a short time frame, it would raise important new directions both for research and for clinical care.

Our study has some important strengths. First, by focusing on recurrent disease, we may have selected a stage of disease that is particularly diet sensitive, a supposition that, if correct, made study of this population resource efficient and may have important potential biological and clinical ramifications. In addition, because men in this study population had few unambiguous clinical options, they may have been highly motivated to engage in dietary change. Second, our intervention employed a variety of elements that may have helped to foster dietary change: individual dietary counseling and follow-up coaching, group-based cooking classes, stress management training to reinforce dietary change, shared model meals, and involvement of spouses/support persons. Third, we used a laboratory test, PSA, which was noninvasive, inexpensive, and familiar to and readily accepted by patients. Because patients had already undergone prostatectomy or radiation therapy, changes in PSA and rates of PSA rise were largely reflective of changes in progressive, systemic disease rather than in localized cancer or noncancerous prostatic conditions. Finally, we employed strict definitions of plant-based food groups. Whereas other studies included partial whole grain products in their definition of whole grains, our definition included only whole kernel grain or 100% whole grain products. Similarly, because we did not wish to dilute the vegetable category with patently unhealthy "vegetables" such as french fries, we deliberately excluded vegetable subgroups such as white potatoes and fried vegetables when calculating total vegetables. Had we used these more relaxed standards, changes in dietary intakes of these food groups would have appeared to be even higher. However, the potential therapeutic impact of these foods would have been correspondingly diminished and made more difficult to detect and appreciate.

Our study also has several limitations. The small sample size limited our statistical power and prevented stratum-specific analyses or meaningful control of covariates. Similarly, the lack of a randomized control group made it harder to be certain of the validity of our findings. Because our intervention incorporated both diet modification as well as stress management training, we cannot easily separate out effects specifically due to either one of these components. Our method of dietary assessment, 24-hour recall, can yield results that are highly variable from day to day or that may suffer from recall bias. Furthermore, the use of only one 24-hour recall at each time point (rather than the generally recommended 3 to 4 at or near each time point) may have diminished the validity of the dietary information on which our findings are based. Finally, because we selected a study population with a medical condition that likely instilled a high level of motivation to participate in our intervention, we may be limited in our ability to generalize findings regarding their dietary changes to the larger prostate cancer patient population.

Conclusions

Our findings suggest that with a motivated patient population (ie, men with recurrent prostate cancer) and a multifaceted intervention, major dietary change can be effected and sustained for a least the short term. Changes in rate of PSA rise, an indicator of disease progression, were in the opposite direction of changes in intake of plant-based food groups, raising the provocative possibility that PSA may have inversely tracked the intake of these foods and perhaps suggesting that patients' prostate cancers may have responded quickly to short-term changes in diet. This also raises the intriguing possibility that diet may play an important, relatively immediate, biological role in the progression of prostate cancer and may also have therapeutic potential in the management of recurrent disease.

A more rigorous clinical trial will be needed to confirm this as well as to address the role of dietary adherence and its relationship to prostate cancer progression. In the future, larger randomized trials will be needed to ascertain whether dietary changes can be maintained for a longer time period and whether these changes can affect clinical outcomes such as time to development of metastases, change in tumor volume, or overall survival.

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