Potential Attenuation of Disease Progression in Recurrent Prostate Cancer With Plant-Based Diet and Stress Reduction

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A rising level of prostate-specific antigen (PSA), after primary surgery or radiation therapy, is the hallmark of recurrent prostate cancer and is often the earliest sign of extraprostatic spread in patients who are otherwise asymptomatic. While hormonal therapy may slightly extend survival in a minority of patients, it is not curative and produces side effects including hot flashes, decreased libido, and loss of bone mass. Alternatively, dietary modification may offer an important tool for clinical management. Epidemiologic studies have associated the Western diet not only with prostate cancer incidence but also with a greater risk of disease progression after treatment. Conversely, many elements of plant-based diets have been associated with reduced risk of progression. However, dietary modification can be stressful and difficult to implement. We therefore conducted a 6-month pilot clinical trial to investigate whether adoption of a plant-based diet, reinforced by stress management training, could attenuate the rate of further PSA rise. Urologists at the University of California, San Diego, and San Diego Veterans Affairs Medical Centers recruited 14 patients with recurrent prostate cancer. A pre-post design was employed in which each patient served as his own control. Rates of PSA rise were ascertained for each patient for the following periods: from the time of posttreatment recurrence up to the start of the study (prestudy) and from the time immediately preceding the intervention (baseline) to the end of the intervention (0-6 months). There was a significant decrease in the rate of PSA rise from prestudy to 0 to 6 months ($P < .01$). Four of 10 evaluable patients experienced an absolute reduction in their PSA levels over the entire 6-month study. Nine of 10 had a reduction in their rates of PSA rise and an improvement of their PSA doubling times. Median PSA doubling time increased from 11.9 months (prestudy) to 112.3 months (intervention). These results provide preliminary evidence that adoption of a plant-based diet, in combination with stress reduction, may attenuate disease progression and have therapeutic potential for clinical management of recurrent prostate cancer.

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

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Prostate cancer is the most common invasive male neoplasm in Western populations. In the United States, 1 man in 6 will develop the disease.[1] Most patients diagnosed with prostate cancer elect to receive some form of definitive primary treatment. Most commonly, this takes the form of radical prostatectomy, although a large number opt instead for radiation therapy. Unfortunately, about 35% of patients will undergo a recurrence of the disease within 10 years of primary treatment.[2] Recurrences are typically marked by a detectable, sustained rise in serum prostate-specific antigen (PSA) from the posttreatment nadir level (the lowest identifiable PSA value after radical prostatectomy or radiation therapy) on successive PSA tests.[2-4] Prostate cancer patients who develop such PSA-defined recurrences after primary treatment are at increased risk of developing clinical evidence of potentially life-threatening metastases.[5,6] However, these PSA elevations typically precede the detection of overt metastases by a relatively long period, often as much as several years. Even in the absence of further treatment, most individuals with recurrences will remain relatively asymptomatic during this interval. Furthermore, for many (such as those who are older or who have very slowly progressive disease), prostate cancer may never advance to the point of becoming a clinical problem. Nonetheless, about a third of those found to have a biochemically defined recurrence will develop radiological or pathological evidence of metastatic spread to bone or visceral organs within the first 5 years of detection of the recurrence. Of these, most will die of the disease within several months to a few years thereafter.[2]

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In most cases, hormonal therapy with agents such as luteinizing hormone-releasing hormone agonists and antiandrogens can suppress disease spread and palliate symptoms of metastases, if and when they develop. In a subset of patients (eg, those with positive lymph nodes or seminal vesicle involvement), its early use may also retard development of metastases and slightly extend overall survival.[7] However, hormonal therapy is not curative,[8,9] and the disease typically becomes refractory within 18 to 24 months.[8] Furthermore, it commonly produces side effects that include hot flashes, loss of libido, gynecomastia, and loss of bone and muscle mass. As a result, many physicians and patients, aware of the limitations of existing treatment options, employ a strategy of active surveillance, typically intervening only when PSA rises at a very rapid rate or to high levels or when clinical signs or symptoms of metastatic disease ensue.[7,8] This has motivated a search for novel approaches without the side effect profile of hormonal agents that could attenuate tumor progression, prevent the development of metastases, and significantly extend overall survival without compromising quality of life.

Diet may constitute one of the most important sets of environmental factors influencing the development and progression of prostate cancer. Consumption of meat and dairy products appears to increase risk, and consumption of plant-based foods appears to decrease risk. In an extensive literature review by Kolonel et al, a positive association of meat intake with prostate cancer risk was identified in 16 of 22 studies.[10] In another review by Chan and colleagues, 12 of 23 studies linked consumption of dairy foods with prostate cancer risk.[11] A possible mechanism of action for both food groups is arachidonic acid, which is synthesized endogenously from omega-6 fatty acids and is also preformed in the cell membranes of animal-based foods. Laboratory studies indicate that arachidonic acid stimulates the growth of LNCaP in both hormone-sensitive and hormone-insensitive cell lines.[12]

Whole grains, vegetables, legumes, and fruits may be protective. Among studies reviewed by Chan et al, 8 of 16 found inverse associations of specific or total vegetable intake with prostate cancer risk, while none reported increased risk. Leafy greens, cruciferous vegetables (cabbage family), tomatoes, carrots, nuts, beans, and legumes were the most protective.[13] This review and 2 population-based studies detected a reduction in prostate cancer incidence from increased consumption of cruciferous vegetables.[14,15] Indole-3-carbinol, found in diets rich in cruciferous vegetables, inhibits the growth of PC3 human prostate cancer cells.[10] Cruciferous vegetables also contain sulforaphane, an isothiocyanate, which has been found to up-regulate phase 2 enzymes in several human prostate cancer cell lines.[16]

Although psychological stress has not been linked to prostate cancer specifically, it has been associated with chronic prostatitis, interstitial cystitis, and other urological conditions.[16] Conversely, stress management training has been shown to modulate neuroendocrine and neuroimmune pathways[17,18] and may have salutary effects on chronic prostatitis.[19] Furthermore, patients with recurrent prostate cancer, facing a difficult and potentially lethal illness, may suffer from stress; "PSA anxiety," marked by feelings of chronic, intense worry, and helplessness regarding rising PSA levels; and related symptoms such as depression and fatigue. Treatment-associated morbidities such as urinary incontinence and loss of libido can severely affect quality of life as well. Stress management training has been shown to be effective both in reducing panic disorder and anxiety[20,21] and in assisting patients to cope with personal, family, and social conflicts that often arise when making difficult lifestyle changes.[22]

We therefore conducted an intensive nonrandomized intervention study for patients with PSA-defined recurrent prostate cancer in which we fostered adoption of a plant-based diet and reinforced this dietary change with stress management training. This article reports on the changes observed in the rate of PSA rise and, by extension, in the rate of disease progression in patients who were enrolled in this intervention. Each patient served as his own control as we compared the rate of rise of his PSA during the prestudy period with his rate during the intervention (0-6 months).

Patients and Methods

Study Design

The University of California, San Diego (UCSD), Healthy Men Study was a prepilot/postpilot 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 influence the progression of recurrent prostate cancer. In this article, we examine the effect of the intervention on the change in the rate of disease progression, as assessed by comparing the rates of PSA rise for the following periods: from the time of posttreatment recurrence to the start of the study (prestudy) and from the time immediately preceding the intervention (baseline) through the end of the intervention (0-6 months).

The Institutional Review Board of the UCSD School of Medicine approved the study protocol for use of human patients in medical research. All participants provided informed consent before being enrolled in the study.

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 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 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. Patients were encouraged to eat a combined volume of plant-based food 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 ten 3-hour group meetings over the 6-month period (once per week during the first month, once per month during months 2-5, and twice during month 6). At most meetings, test 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 and spouses/support persons were also taught how to practice meditation as well as how to perform several basic yoga and tai chi movements. Stress reduction activities and supportive group discussions were led by a clinical psychologist who was also trained in family therapy, tai chi, and yoga and by an oncology nurse trained in meditation. Patients were also encouraged to engage in the daily practice of 1 or more of these disciplines for at least 15 minutes per day. Group meetings were more frequent initially to assist patients in implementing the diet and stress reduction changes during the initial transition period, but meetings then decreased in frequency when their role was to maintain those changes.

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 were counseled regarding any specific questions or concerns.

Measurements

Data Collection, Assessments, and Phlebotomy

Data collection and assessments, as well as phlebotomy, were performed at the UCSD General Clinical Research Center. 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, 3 months, and 6 months and was used for determination of study-period PSA levels.

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. Rising PSA was confirmed on the basis of a minimum of 3 consecutive individual PSA elevations, at least 1 month apart, starting at the end of the posttreatment nadir. The results of all available prestudy PSA tests, including the 3 tests that documented the PSA rise as well as all tests that followed (up to but not including baseline), were included in determining the prestudy rate. Therefore, the number of PSA tests used to calculate the prestudy rate, as well as the time intervals between these tests, varied between patients. In most cases, all

Table 1. Clinical Characteristics of Each Patient Enrolled

Patient Number	*Tumor Stage*	*Gleason Score*	*Primary Treatment*	*Time Since Primary Treatment (mo)*
1	T2	9	RP	68
2	T3	7	RP	52
3	T3	9	RP	34
4	T1	5	RP	149
5	T2	6	RP	34
6	T1	7	RT	37
7	T1	6	RT	21
8	T3	7	RP	46
9	—	—	—	—
10	T2	7	RP	13
11	T3	6	RP	72
12	T2	5	RP	158
13	T1	8	RT	43
14	T2	8	RP	40

RP = radical prostatectomy; RT = radiation therapy. Patient 9 withdrew at baseline; therefore, clinical data were not available.

prestudy PSA tests were performed at the same laboratory using the same test kit. In cases in which more than 1 laboratory or test kit had been used, only the test results from the laboratory and test kit at which the PSA rise had been first documented were used to calculate a patient's prestudy rate of PSA rise (ie, results from different laboratories and/or test kits were not combined).

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

Statistical Methods

Descriptive statistics were tabulated for patients' disease and treatment characteristics at baseline. The rate of rise in PSA for each patient was calculated within each study period using linear regression modeling of the natural logarithm of PSA over time (months). PSA doubling time for each patient was calculated within each study period as the natural logarithm of 2 divided by the rate of rise in PSA. Medians (and ranges) were tabulated for the rate of rise in PSA and doubling time for the following study periods: prestudy and 0 to 6 months. Paired comparisons were made using the Wilcoxon signed-rank test. All analyses were conducted using SAS (version 8.01; SAS Institute Inc, Cary, NC, 2000).

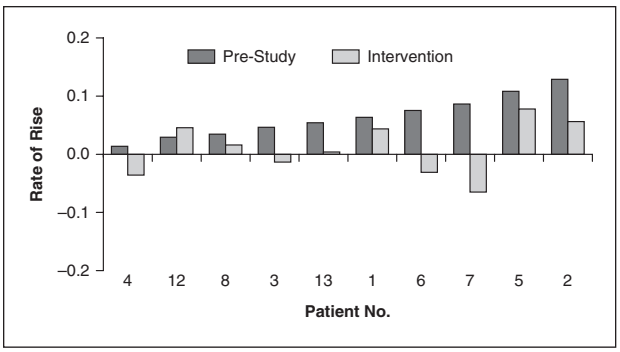

Figure 1 Rate of rise in prostate-specific antigen for each patient by study period.

Results

Table 1 shows the clinical characteristics including type of primary treatment used prior to intervention.

Fourteen patients were enrolled. Immediately after enrollment, 1 elderly patient withdrew from the study prior to his baseline visit, so his data are not available. Of the 13 patients who participated in the study, 8 had moderate to high Gleason scores and 10 had a radical prostatectomy. The median length of time from primary treatment to the start of intervention was 43 months (range, 13-158 months). The length of the intervention was 6 months.

Only 10 of the 13 patients were evaluable by the end of the study; patients 10 and 14 reported using hormonal 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.

Of the 10 evaluable patients, 5 had a decrease in absolute serum PSA levels at 3 months and 4 had a decrease at 6 months. Figure 1 shows the rate of rise in PSA for each of the 10 patients by study period (prestudy and 0-6 months).

The rate of rise in PSA was significantly less during the dietary intervention (0-6 months) than prior to the study ($P < .01$, Wilcoxon signed-rank test). Overall, 9 of the 10 patients showed a decrease in the rate of rise in PSA; 4 of the 9 had negative PSA rates, indicating an overall reduction in their PSA levels.

Table 2. Prostate-Specific Antigen Doubling Time of Each Patient by Study Period

	Doubling Time in Months	
Patient Number	*Prestudy*	*0-6 Mo*
1	10.9	15.9[a]
2	5.4	12.4[a]
3	14.9	–52.0[a]
4	50.5	–19.3[a]
5	6.4	8.9[a]
6	9.2	–22.4[a]
7	8.0	–10.7[a]
8	20.0	43.6[a]
12	23.7	15.2
13	12.8	180.9[a]

a. Improved prostate-specific antigen (PSA) doubling time compared to the doubling time prior to study intervention. Negative PSA doubling time reflects overall reduction in PSA level (halving time).

Table 2 shows the doubling time of PSA for each of the 10 patients by study period (prestudy and 0-6 months).

Nine of 10 patients showed an improvement in their PSA doubling times compared to the doubling times prior to study intervention. Four of the 9 patients had negative doubling times for the 6-month intervention period, reflecting their overall reductions in PSA. Patient 12 did not show an improvement; his doubling time decreased from 23.7 to 15.2 months. The median PSA doubling time increased from 11.9 months (range, 5.4-50.5) prior to the intervention to 112.3 months (range, doubling time of 8.9 to a halving time of 10.7 months).

Of the 4 patients who had negative doubling times, patient 7 experienced the fastest decline in absolute PSA (doubling time of –10.7). At this rate, it would take his PSA 10.7 months to be reduced by 50%. Patient 3, with a doubling time of –52.0 months, also experienced a decline but at the slowest rate among the patients with negative doubling times. Of the 6 patients who had positive doubling times, patient 5, with a doubling time of 8.9 months, experienced the fastest rate of PSA rise over the 6-month intervention period. Conversely, patient 13, with a doubling time of 180.9 months, experienced the slowest rate of rise.

Discussion

This study investigated the change in a marker of disease progression, the rate of PSA rise, in patients with recurrent prostate cancer who were enrolled in an intensive plant-based diet and stress reduction intervention. We observed a significant reduction in the rate of PSA rise during the 6-month intervention period from prestudy. By the end of the intervention, 4 of 10 patients experienced an absolute reduction in their PSA levels and 9 of 10 experienced a decrease in the rate of further PSA rise. Median PSA doubling time increased from 11.9 months (prestudy) to 112.3 months (intervention).

After recurrence, a rising PSA level is a strong indicator of the existence of extraprostatic micrometastases, and the rate of further PSA rise is the best single predictor of survival. The rate of PSA rise is also the best predictor of the risk of developing overt metastases as well as the time to their formation. For example, those with a PSA doubling time less than 10 months have a 65% to 75% 5-year risk of developing metastatic disease, whereas those with doubling times greater than 10 months have a risk of only 10% to 20%.[23] While there are some circumstances in which rising PSA after posttreatment nadir might not result from the spread of extraprostatic disease (eg, presence of residual normal prostatic tissue inadvertently spared during prostatectomy, transient postradiation PSA "bounce" resulting from radiation-induced prostatitis, or variability inherent in the PSA test), these do not likely affect our findings. To limit the likelihood that any of our patients' PSA rises were due to anything other than extraprostatic spread of prostate cancer, we confirmed at least 3 consecutive increases in PSA after post primary treatment nadir. This is consistent with the recommendations of a consensus of experts from the American Society for Therapeutic Radiology and Oncology.[24]

Our findings suggest that the intervention we employed may have resulted in a slowing of disease progression and, in a few patients, possibly disease reversal. For many years, the prevailing scientific consensus has been that cancer progression is largely irreversible and that treatment needs to be eradicative. Our findings do not refute the benefits of standard therapies or guarantee that a plant-based diet and stress reduction will always induce remission. But they do contribute to a growing literature that suggests that in at least some circumstances, cancer may be partly reversible and that modification of dietary and lifestyle factors may be able to help prevent disease spread.

In the largest study to date of the natural history of recurrent prostate cancer, lower PSA doubling times (<10 months) were associated with a shorter time to development of clinically evident metastases.[2] The interruption or limitation of further disease progression, if it could be sustained, would potentially avert or delay the development of overt metastases and resultant disease-related symptoms and premature death from prostate cancer. By contributing to an increase in doubling time and slowing of disease progression, dietary modification and stress reduction

could become a viable long-term therapeutic adjunct to active surveillance and an adjunct or alternative to hormonal therapy.

The magnitude of effect of our findings is the strongest observed to date among dietary and nutritional interventions with pre-post study designs undertaken in recurrent prostate cancer. In an earlier 4-month intervention trial that also emphasized a plant-based diet and stress reduction, Saxe et al found a significant reduction from prestudy in the rate of PSA rise and a concomitant increase in median PSA doubling time from 6.5 to 17.7 months.[23] In a trial that focused on supplementation with 2000 IU/d of cholecalciferol (vitamin D3), Woo et al found a significant reduction in the rate of PSA rise during the intervention in comparison with the prestudy period, as well as an increase in median PSA doubling time from 14.3 months to 25 months.[26] Two other trials involved administration of calcitriol, a synthetic vitamin D analog. Gross et al found a significant reduction in the rate of PSA rise when using a maximum dose of 2.5 μg/d.[25] However, administration was limited by dose-dependent hypercalciuria. This study did not report on the change in PSA doubling time.[26] In a study by Beer et al in which patients maintained a calcium-limited diet and calcitriol was administered at a dose of 0.5 μg/kg once per week, median PSA doubling time increased significantly from 7.8 months to 10.3 months without hypercalcemia or other dose-limiting toxicities.[27]

It is not clear why we observed such a strong magnitude of effect in comparison with other studies. One possibility is that modification of the overall dietary pattern resulted in altered intake of an array of nutritive and nonnutritive compounds, not merely 1 targeted nutrient such as vitamin D. It is possible that synergistic interactions between these compounds were achieved and that this may have had far more profound effects on prostate cancer carcinogenesis and disease progression than change in a solitary nutrient. But why was the magnitude of effect in the UCSD study stronger than the effect observed earlier in the study at the University of Massachusetts? Both studies attempted to foster adoption of a plant-based diet and reinforced this change with stress reduction. The longer length of the UCSD intervention does not explain its relatively stronger magnitude of effect given that in a separate analysis, we found that the strongest effects of the UCSD intervention were observed for the period of 0 to 3 months. One possible explanation is that the UCSD study may have achieved a greater degree of dietary change than the earlier study at the University of Massachusetts. Although the 2 interventions had a roughly equal schedule of group meetings and both encouraged the participation of a spouse or support person, the UCSD study established more ambitious dietary goals and provided telephone counseling. Of course, it is also possible that the differences resulted from non-treatment-related effects such as differences in the patient populations.

All of these nutritional approaches, including ours, were based on pre-post study designs. It is therefore possible that all could have shared a common problem: their reported beneficial effects on PSA doubling time could be accounted for by a purported tendency of the rate of PSA rise to naturally attenuate over time, perhaps decreasing with an expanding volume of cancer within the body. However, the scientific literature suggests otherwise. In the absence of treatment, absolute levels of PSA tend to increase exponentially, while the rate of PSA rise usually remains constant, that is, linear on a logarithmic scale.[2] Two of the earlier nutritional studies[23,24] further addressed this issue by testing the assumption that the rate of rise in PSA would remain constant. In these studies, prestudy PSA readings (taken prior to their respective nutritional interventions) were divided into 2 time periods: early-pre and late-pre. Rates of PSA rise and doubling times were calculated for each of these 2 time periods and examined for differences using Wilcoxon signed-rank tests for paired comparisons. No significant differences were detected, reinforcing the perspective that the rate of disease progression was independent of the volume of disease, at least in the context of the moderately low PSA levels seen in each of those studies.

One possible advantage of our approach over the earlier vitamin D trials is that both a plant-based diet emphasizing whole grains and vegetables and stress reduction are essentially devoid of potential toxicity. Conversely, supplemental vitamin D and the synthetic vitamin D analog calcitriol have at least a theoretical potential for toxic side effects such as hypercalcemia and formation of renal calculi. In contrast, not only is the approach we employed apparently beneficial for prostate cancer, but it has therapeutic benefits that may extend to a variety of comorbidities (eg, diabetes, hypertension, cardiovascular disease, and possibly other cancers) facing a population of middle-aged or older men. Balanced against these advantages are the possible burdens and restrictions placed on patients. Diet and lifestyle changes are not easy to implement and may need to be maintained for a lifetime. However, a large subset of patients with recurrent prostate cancer may be especially motivated to make such changes, particularly given the limitations of other available therapeutic options. Furthermore, there may be reinforcement by secondary gains such as the feeling of personal empowerment, sense of physical well-being, or enhancement of quality of life they may experience when implementing these changes.

Our study had some important strengths. By focusing on recurrent prostate cancer, we selected a stage of disease that may be particularly diet sensitive, a supposition that, if correct, makes study of this population resource efficient and may have important potential biological and clinical ramifications. Since men with recurrent disease have few unambiguous clinical options, they are inherently motivated to consider alternative therapies such as dietary change. We used a laboratory test, PSA, which is noninvasive, inexpensive, and readily accepted by patients. In the setting of recurrent prostate cancer, changes in absolute PSA levels and the rate of PSA rise were largely reflective of changes in progressive, extraprostatic disease rather than in localized cancer or noncancerous conditions of the prostate. Finally, our intervention employed a variety of elements (eg, involvement of spouses, stress management training, cooking classes, telephone counseling) that may have helped to foster dietary change.

Our study has some limitations. The small sample size prevented stratum-specific analyses and meaningful control of covariates. The period of intervention was relatively short, and it is uncertain how enduring the effects would be after 6 months even if the intervention had continued. Finally, this study did not have a randomized control group, and the potential exists for selection or other biases that could affect the validity of findings or their generalizability.

Conclusions

Our findings provide preliminary evidence that adoption of a plant-based diet, in combination with stress reduction, may attenuate disease progression. Over the course of the 6-month intervention, there was a significant decrease in the rate of PSA rise from the prestudy period. Four of 10 patients experienced an absolute reduction in their PSA levels, suggesting the possibility of at least some degree of disease remission. Nine of 10 had a reduction in their rates of PSA rise and an improvement of their PSA doubling times, suggesting a consistent slowing of the progression of disease. The increase in median PSA doubling time, from 11.9 months (prestudy) to 112.3 months (intervention) is the largest that has been reported in any dietary or nutritional intervention trial in recurrent prostate cancer. These findings have considerable therapeutic potential for the clinical management of recurrent prostate cancer, raising the possibility that a natural dietary and lifestyle-based approach may serve as an adjunct to active surveillance and an adjunct or alternative to hormonal therapy. In the future, larger randomized trials will be needed to ascertain how to best promote long-term adherence to these behaviors 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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