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The Effects of a Plant-Based Diet and Stress Reduction Techniques on PSA Doubling Time in Prostate Cancer Recurrence

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The Effects of a Plant-Based Diet and Stress Reduction Techniques on PSA Doubling Time in Prostate Cancer Recurrence

Abstract

Background: Prostate cancer is the most common cancer affecting men. It is also very common for men to suffer from recurrence after primary therapy is completed. The current most commonly used therapies for prostate cancer recurrence, hormonal therapy and radiation, have significant side effects. It is known that diet influences cancer prevention, progression, and recurrence. A plant-based diet, especially when combined with stress reduction techniques, may be a useful therapeutic option with fewer side effects for men with recurrent prostate cancer. This review examines the effects of a plant-based diet and stress reduction on PSA doubling time in prostate cancer recurrence.

Methods: An exhaustive search of available medical literature was performed using MEDLINE-PubMed, Web of Science, and SagePub Journals. Keywords used included: prostate specific antigen, PSA, recurrent, doubling time, prostate-healthy diet, plant based diet, vegetable proteins, prostate cancer, and prostatic neoplasm. Studies were assessed for quality using GRADE criteria.

Results: Thirteen articles were identified with the search strategy. Four of these articles were found to be relevant, including 1 RCT and 3 observational studies. All 4 studies reported an increase in PSA doubling time; 3 of the 4 study results were found to be statistically significant. The quality of the studies ranged from low to very low and further research is necessary to follow larger groups of patients for a longer interval before these results can be extrapolated to the larger populations.

Conclusion: A plant-based diet in combination with stress reduction techniques is not a reliable method of therapy for all patients with recurrent prostate cancer. However, there is no potential for harm, and current research shows potential benefits, with some men responding better than others.

Keywords: Prostate specific antigen, recurrent, doubling time, prostate-healthy diet, plant based diet, vegetable proteins, prostate cancer, prostatic neoplasm

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prostate specific antigen, doubling time, plant based diet, prostate cancer, recurrent, vegetable proteins

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**The Effects of a Plant-Based Diet and Stress Reduction
Techniques on PSA Doubling Time in Prostate Cancer
Recurrence**



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&
Jacob McAvoy

***A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies***

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Biography

Amanda Barclay is an Oregon native, who graduated from the University of Oregon with a degree in Human Physiology. After graduating in 2015, she worked in Eugene, Oregon as a medical scribe for nearly two years in primary care and urology before attending PA school.

Jacob McAvoy is a native of Oregon and graduated from the Oregon Institute of Technology in 2017 with a degree in Biology & Health Sciences. While at OIT, he was involved in undergraduate research and worked as a certified nursing assistant (CNA)/medication aide. He started PA school immediately after graduating from OIT.

Abstract

Background: Prostate cancer is the most common cancer affecting men. It is also very common for men to suffer from recurrence after primary therapy is completed. The current most commonly used therapies for prostate cancer recurrence, hormonal therapy and radiation, have significant side effects. It is known that diet influences cancer prevention, progression, and recurrence. A plant-based diet, especially when combined with stress reduction techniques, may be a useful therapeutic option with fewer side effects for men with recurrent prostate cancer. This review examines the effects of a plant-based diet and stress reduction on PSA doubling time in prostate cancer recurrence.

Methods: An exhaustive search of available medical literature was performed using MEDLINE-PubMed, Web of Science, and SagePub Journals. Keywords used included: prostate specific antigen, PSA, recurrent, doubling time, prostate-healthy diet, plant based diet, vegetable proteins, prostate cancer, and prostatic neoplasm. Studies were assessed for quality using GRADE criteria.

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Conclusion: A plant-based diet in combination with stress reduction techniques is not a reliable method of therapy for all patients with recurrent prostate cancer. However, there is no potential for harm, and current research shows potential benefits, with some men responding better than others.

Keywords: Prostate specific antigen, recurrent, doubling time, prostate-healthy diet, plant based diet, vegetable proteins, prostate cancer, prostatic neoplasm

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Table 1. Quality Assessment of Reviewed Studies

List of Abbreviations

PSA	Prostate Specific Antigen
MBSR	Mindfulness Based Stress Reduction
QOL	Quality of Life

The Effects of a Plant-Based Diet and Stress Reduction Techniques on PSA Doubling Time in Prostate Cancer Recurrence

BACKGROUND

Prostate cancer is the most common cancer in men, accounting for 28% of all cancers. Prostate cancer is also the second most common cause of cancer-related deaths in males.¹ In the United States, 1 in 6 men will be diagnosed with prostate cancer, and 35% will experience a recurrence within 10 years of primary treatment.²

To date, there has been a substantial amount of preliminary research into the dietary components of cancer prevention and treatment. Past studies³ have shown the association between various diets and their role in cancer prevention and treatment. The plant-based diet intervention is of great interest in prostate cancer specifically as an adjunctive, or even replacement, therapy for hormonal therapy.

Hormonal therapy is commonly used as first-line therapy for men with recurrent prostate cancer after primary intervention. Hormonal therapy options such as bilateral orchiectomy, estrogen therapy, luteinizing hormone-releasing hormone agonist therapy, and antiandrogen therapy are associated with many unfortunate side effects. These side effects include loss of libido, hot flashes, osteoporosis, gynecomastia, and impotence.⁴ The utilization of a dietary intervention in adjunct to or as a replacement for these therapies could potentially help reduce the occurrence of these unfavorable side effects that have obvious negative effects on patients' quality of life.

One well-recognized limitation of a dietary intervention as a treatment is that it can be difficult to adopt a new diet, especially in the face of a stressful cancer diagnosis. Therefore, there is interest in the effects of changing to a plant-based diet in combination with stress

reduction techniques to help the patient adjust to the adoption of a new diet. A combined intervention of a plant-based diet and stress reduction techniques may be effective at preventing recurrence of prostate cancer in patients with rising PSA levels after primary treatment.

METHODS

An exhaustive literature search using MEDLINE-PubMed, Web of Science, and SagePub Journals was done using the search phrase: ("prostate specific antigen" OR PSA) AND recurrent AND "doubling time" AND ("prostate-healthy diet" OR "plant based diet" OR "vegetable proteins") AND ("prostate cancer" OR "prostatic neoplasm"). Both authors conducted separate searches using these parameters. They included studies that researched men with recurrent prostate cancer that followed an intervention of a plant-based diet and stress reduction techniques in comparison to watchful waiting, and measured the change in PSA doubling time. Relevant articles were evaluated for quality using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group guidelines.⁵

RESULTS

The search initially produced 13 results. After screening these results for duplicates and reviewing the remaining articles using the aforementioned eligibility criteria, a total of 4 relevant articles were identified. One article was a randomized control trial⁶ and the remaining 3 studies were observational pre-post study designs.^{7,8,2} (See Table 1.)

Carmody et al

This randomized control trial⁶ investigated the effects of a diet high in plant-based foods and fish in conjunction with integrated mindfulness practice on quality of life (QOL) and prostate-specific antigen (PSA) velocity in men with recurrent prostate cancer. The study took

place in the United States and included 36 men with an increasing PSA level who had previously undergone primary therapy for biopsy-confirmed prostate cancer. The participants did not receive any additional treatment in the 6-months prior to the start of the study. The majority (91%) of participants were non-Hispanic white men with an average age of 69.1 years (SD 9.0). Participants had an average time from primary treatment of 5.3 years (SD 3.0). One week prior to the start of the study, the 36 participants were randomized into an intervention (n=17) and control group (n=19). According to the authors of the study, both groups were prognostically balanced at the start of the trial.⁶

The intervention consisted of 11 weekly 2.5-hour classes. The classes were held at the University of Massachusetts Medical School teaching kitchen and taught patients how to shop for and cook meals that were adherent to the desired study diet. The diet was focused on increasing vegetables, whole grains, soy foods, and fish, and encouraged avoidance of meat, poultry, and dairy. These classes also incorporated the use of mindfulness as a method of coping with the stress of a dietary change. To supplement these weekly classes, the participants were also given several resources to use at home, including a cookbook and mindfulness CD. Spouses were encouraged to provide support to the participants throughout the trial. The control group consisted of the usual standard of care, watchful waiting.⁶

Of the 17 men in the intervention group, 10 were followed through the entirety of the study. Of the 19 men in the control group, 14 were followed through the entirety of the study. Outcomes included adherence to dietary intake, mindfulness practice, quality of life, and change in PSA. While these 4 variables were measured, only the change in PSA is pertinent to the clinical question. PSA was checked at baseline and 3 months after completion of the intervention. At baseline, mean PSA level was 2.96 ± 4.51 ng/mL and there was no statistically significant difference between the mean PSA levels of the intervention and the control group. At

3-months after intervention, there was no statistically significant difference found between the intervention and control group for the rate of PSA increase. However, the mean PSA doubling time for the intervention group increased from 21.5 months (95% CI 12.8-66.8) to 58.5 months (95% CI 14.7-∞) at 3-months post intervention. This was substantially longer compared to the control group with values of 18.4 months (95% CI 12.1-39.2) to 18.7 months (95% CI 10.6-81.0) at baseline and 3-months post intervention, respectively.⁶

Limitations of the study included a small study size and participant withdrawal, lack of blinding and allocation concealment, and imprecision. The researchers note “budgetary and time-line constraints” that made it difficult to recruit the number of participants the study was originally designed for.⁶

Nguyen et al

This observational, pre-post design study⁷ examined the effects of a plant-based diet and stress reduction on PSA doubling time in men with recurrent prostate cancer. The study took place in the United States and consisted of 14 men with prior biopsy confirmed prostate cancer that had undergone primary treatment and were experiencing rising PSA and had not used hormonal therapy within the last 12 months. The participants were predominantly Caucasian (85%) with a median age of 70 years.⁷

The participants’ education on dietary changes emphasized increasing their intake of whole grains and vegetables. The secondary goals were to increase intake of fruit and legumes and to decrease consumption of meat, dairy, and refined carbohydrates. Participants, as well as their spouses, attended 10 scheduled 3-hour group meetings over 6 months. These meetings included participation in a hands-on cooking demonstration, consumption of an intervention compliant meal, group discussion, and instruction on meditation, tai chi, and yoga techniques for stress reduction. Patients were instructed to practice at least 1 or more of the stress

reduction techniques daily and received phone calls weekly for additional guidance and support.⁷

Of the 14 men eligible for the study, 10 were followed through the entirety of the study. Outcomes included adherence to dietary intake and change in PSA. These outcomes were measured at baseline, 3 months, and 6 months. The participants were able to make the dietary adjustments evidenced by an increase of whole grains of 306% at 3 months and 194% at 6 months; an increase in vegetables of 79% at 3 months and 71% at 6 months. The rate of rise in PSA decreased substantially as seen in the following trend: median rate of PSA rise at baseline = 0.059 (0.014-0.129); at 3 months = -0.002 (-0.096-0.079) indicating a significant decrease and reduction in the absolute PSA value; at 6 months = 0.029 (-0.067-0.136).⁷

Limitations of the study included a small study size of only 10 participants, lack of a randomized control group, and a short duration of 6 months. The researchers also note that the reduction in PSA rise could be due to decreased intake of another food group such as meat or dairy rather than the increase in vegetables and whole grains.⁷

Saxe et al 2001

This observational study⁸ explored the effects of a plant-based diet in combination with Mindfulness Based Stress Reduction (MBSR) on the rate of change of PSA in men with recurrent prostate cancer. The study took place in Massachusetts and included 10 men with rising PSA levels after primary treatment for biopsy confirmed prostate cancer. Study participants were excluded if they had received primary high dose radiation therapy, post-operative radiation, or hormone therapy within the 6 months prior to the trial. Men were also excluded if they had received more than 1 Lupron injection in the year prior to the study. Participants had an average age of 67.4 years (SD 6.32). The men served as their own control in a pre-post study design. The doubling time and rate of change of PSA prior to and after intervention was observed.⁸

The dietary intervention included increasing fiber, whole grains, legumes, green and yellow vegetables, seeds, soy, and fruit, while decreasing saturated fat, processed food, and foods with animal byproducts. The MBSR aspect included training in mindfulness meditation, yoga, and social support. Prior to the group intervention, the participants received individual MBSR orientations and dietary counseling. The group intervention included 12 weekly classes that were each 3-4 hours long. A spouse or support person was required to attend classes with the participants. The weekly classes included education in cooking and MBSR training.⁸

All 10 men eligible for the study completed the study. Outcomes measured included PSA, total fat intake, fiber intake, and caloric intake. In 8 men, there was a decreased rate of PSA change and 3 of those men also had an absolute decrease in PSA levels. The slope of PSA change increased in 2 men, but overall there was a statistically significant decrease of the slope of PSA change in the group as a whole. PSA was checked at baseline and then again after the 4-month intervention. The mean pre-study PSA doubling time was 6.5 months (95% CI 3.7-10.1), which increased to 17.7 months (95% CI 7.8-infinity) after the 4 month intervention.⁸

One limitation of this study is the small sample size of 10 participants. It was also an observational study with a pre-post design rather than a randomized control trial with a true control group. The duration of the study was also short at only 4 months, which is another limitation.

Saxe et al 2006

This observational, pre-post study² investigated the effects of a plant-based diet in combination with stress management on the rate of rise in PSA in men with recurrent prostate cancer. The study took place in the United States and consisted of 14 patients with prior biopsy confirmed prostate cancer that had undergone primary treatment and were experiencing rising PSA and had not used hormonal therapy within the last 12 months.²

The dietary intervention had an emphasis on teaching the participants to increase intake of whole grains, vegetables, fruit, and legumes. The secondary goal was to decrease consumption of meat, dairy, and refined carbohydrates. Participants, along with their spouses, attended 10 separate 3-hour group meetings over a 6-month period. These meetings consisted of a hands-on cooking demonstration, group discussions, and instructions on meditation, tai chi, and yoga techniques for stress reduction. The patients were asked to perform at least 15 minutes of these stress reduction techniques daily. For additional support, the participants received a baseline orientation, individual dietary counseling, instructional materials for at-home reference, and weekly telephone calls.²

Of the 14 men originally enrolled in the study, 10 were followed through to completion of the study. The PSA values were measured at baseline, 3 months, and 6 months. At 3 months, 5 patients had a decrease in their absolute serum PSA levels relative to their baseline levels. At 6 months, 4 patients had maintained that decrease in their absolute PSA levels. Overall, 9 of the participants showed an increase in their PSA doubling time. Median PSA doubling time increased from 11.9 months (range, 5.4-50.5) at baseline to 112.3 months (range, doubling time of 8.9 to a halving time of 10.7 months). There was 1 outlier whose PSA doubling time decreased from 23.7 months to 15.2 months at baseline and 6 months, respectively.²

Limitations of the study included a small study size of only 10 patients, lack of randomized control group, and a short duration of 6 months.²

DISCUSSION

Prostate cancer affects many men, and there are expected to be 174 650 new prostate cancer diagnoses and approximately 31 620 prostate cancer deaths in 2019.⁹ Current treatments for recurrent prostate cancer consist mainly of various hormonal therapies and radiation therapy, both of which are associated with numerous side effects. There has been

increasing interest in alternative options for recurrent prostate cancer. Among these, a plant-based diet is being researched.

The 4 studies^{2,6-8} identified in this systematic review explored the effects of a plant-based diet and stress reduction techniques on PSA doubling time in men with recurrent prostate cancer. Clinically, the current most commonly used marker for prostate cancer is PSA. All 4 studies^{2,6-8} showed prolonged PSA doubling times with the combination of stress reduction techniques and a plant based diet, but only 3 of the 4 studies^{2,7,8} reported statistically significant results. These studies were evaluated for quality using the GRADE method, which can be seen in Table 1.

While these studies seem promising, due to the small sample sizes and lack of blinding and true control groups, it's difficult to extrapolate these results into a larger population. Across all studies, there were small sample sizes, which limit the statistical power and precision, and there was a lack of blinding and allocation concealment, which may introduce bias. At most, the studies were only done for 6 months, so clinicians are unable to determine if the results are still significant past that time-period. Additionally, 3 out of 4 of the studies^{2,7,8} utilized a pre-post study design and were not randomized controlled trials, which weakens the evidence.

Recommendations for further study include using a larger sample size, continuing the study for a longer time-period, and conducting a randomized control trial. While PSA is used clinically to screen for and monitor prostate cancer, it would also be beneficial to perform a study that measures additional outcomes such as metastasis and overall mortality. As discussed in one study,⁷ it's unclear if the PSA doubling time increases due to an increased intake of vegetables, legumes, and whole grains, or because of the subsequent decrease in meat and dairy consumption, so this warrants more investigation.

From the current analysis, it appears that the effectiveness of a plant-based diet and stress reduction techniques in preventing prostate cancer recurrence is highly patient dependent. However, there is no potential for harm from these techniques. Patients that would be most likely to benefit include those who are interested in making these dietary and lifestyle changes and have sufficient support systems in place to assist with the transition and ensure it is long-lasting. Clinicians should discuss adoption of a plant-based diet and stress reduction techniques as treatment alternatives or as adjunctive therapy with applicable patients and employ shared decision making techniques to identify which patients would be most likely to benefit.

CONCLUSION

Prostate cancer is the most common cancer affecting men¹ and the current treatment options for recurrent prostate cancer have many unpleasant side effects. A plant based diet in combination with stress reduction techniques may be an option for certain men in need of treatment for recurrent prostate cancer. From the current research, it does not appear that stress reduction techniques in conjunction with a plant-based diet will reduce the recurrence of prostate cancer reliably in everyone, but they may be used adjunctively. However, there is no potential for harm by making these dietary and lifestyle changes, and the results of the studies point towards potential benefits. The benefits are variable, and some men seem to respond better than others.

Since it can be difficult to make these drastic life changes, especially for older men, this may not be an appropriate therapy for unmotivated or unsupported individuals. If men are interested in making these dietary and lifestyle changes, this may be an option to slow the rate of PSA doubling time in prostate cancer recurrence. The incorporation of stress reduction techniques may make the adjustment process easier and longer-lasting. However, more studies

are needed to further elucidate the extent of the benefits that men with recurrent prostate cancer may experience by changing to a plant-based diet and incorporating stress reduction techniques.

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Table 1: Quality Assessment of Reviewed Studies

Study	Design	Downgrade Criteria					Upgrade Criteria	Quality
		Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		
Carmody et al ⁶	RCT	Not serious ^a	Not serious	Not serious	Serious ^{b,c}	Unlikely	None	Low
Nguyen et al ⁷	Observational	Serious ^d	Not serious	Not serious	Serious ^{b,e}	Unlikely	None	Very Low
Saxe et al 2001 ⁸	Observational	Not serious	Not serious	Not serious	Serious ^b	Unlikely	None	Low
Saxe et al 2006 ²	Observational	Not serious	Not serious	Not serious	Serious ^b	Unlikely	None	Low

^aLack of blinding of data collectors and allocation concealment; however, outcome measures were objective and unlikely influenced by lack of blinding
^bSmall study size
^cLarge confidence intervals due to smaller sample size than the study was originally powered for
^dThe 24-hour recall used to evaluate their adherence to the dietary intervention may be unreliable
^eUpper limit of the confidence interval was greater than the pre-study confidence interval upper limit, which signifies a potentially faster PSA doubling time in the intervention group