Is it necessary to cure prostate cancer when it is possible? (Understanding the role of prostate inflammation resolution to prostate cancer evolution)

Ronald E Wheeler

Prostatitis & Prostate Cancer Center, Sarasota, Fl, USA

Objective: Definitive therapy with radical prostatectomy, cryotherapy, or radiation therapy generally follows the initial diagnosis of prostate cancer, particularly when men have at least 10 additional years of life expectancy. There is growing concern regarding the optimal conservative treatment for patients who decline or do not otherwise qualify for such definitive curative treatment. For those patients who choose a watchful waiting approach, it would be beneficial to know what specific dietary and nutritional methods could potentially slow the progression of their disease. In this prospective study, it was our goal to analyze the efficacy and safety of treating prostate cancer conservatively using the principles of a Mediterranean diet in association with a specific prostate nutritional supplement.

Method: Twenty-three men aged 43–74 (median age: 64) with biopsy proven, organ-confined prostate cancer who had already declined immediate hormonal therapy and attempts at a curative cancer treatment agreed to participate in a Chronic Disease Management (CDM) protocol highlighted by diet with a specific prostate nutritional supplement. The diet recommended was a modified Mediterranean diet while a patented nutritional prostatitis formula (Peenuts®) was the supplement common to all patients. Prostate specific antigen (PSA), a recognized marker of prostate disease and prostate cancer activity, was the primary indicator to validate exacerbation or suppression of disease. All men were followed with serial PSA testing, a digital rectal exam, an International Prostate Symptom Score index (IPSS-Index) and an expressed prostatic secretion (EPS) examination. The primary Gleason sum/score represented in this study was 6 (n = 11), while Gleason sum patterns 5, 5/6, 6/7, and 7 were also evaluated. Referencing the Partin Tables, organ confinement was predicted to be 66%.

Results: Eighty-seven percent of men (n = 20) noted a 58% reduction (range of improvement: 13%–90%) in PSA over an average of 38.5 months (range: 13–84 months). The remaining 13% of men included three men who experienced a mild elevation in PSA of 0.3 ng/ml, 0.7 ng/ml, and 0.9 ng/ml over 14 months, 42 months, and 34 months, respectively. Fifteen men had completed an initial and secondary IPSS-Index while 14 men had undergone an initial and secondary EPS. The mean percentage reduction in IPSS-Index was 61% (range: 20%–100% with a median of 55%), while men evaluated with EPS examinations noted a mean percentage reduction in white blood cells of 77.5% (range: 33%–99% with a median of 82%). These results were evaluated using the t-test, Wilcoxon Analysis and the Null Hypothesis and found to be statistically significant.

Conclusion: Clearly there is a need to develop effective alternative conservative therapies for the increasing numbers of prostate cancer patients who will not tolerate definitive curative measures or simply choose a conservative approach. Although this prospective study had no control arm, was of limited duration and included only 23 participants, it did appear to show significant benefit to the majority of prostate cancer patients treated with selective nutritional and dietary therapy alone. Such treatments may provide a safe and effective long-term treatment alternative for some patients. Further study is encouraged.

Keywords: Prostate cancer, prostatitis, prostate cancer nutrition, PSA, EPS, Gleason score, voiding symptoms, Mediterranean diet

Correspondence: Ronald E Wheeler, The Prostate Cancer Center, 1250 South Tamiami Trail, Suite One North, Sarasota, Florida 34239, USA
Tel +1 941 957 0007
Fax +1 941 957 1033
Email prostadoc@aol.com

Prostate cancer is the most commonly diagnosed malignant neoplasm among men in North America (Greenlee et al 2001). Notwithstanding the strides that have been made related to diagnosis and treatment, prostate cancer still poses a significant health risk. In 2005, the incidence of prostate cancer was noted to be in excess of 232 000 new cases while prostate cancer death currently ranks as the second most common male cancer death with approximately 32 000 men dying from the disease (ACS 2004). According to the SEER (Surveillance, Epidemiology & End Result) data and the age specific population projections in association with the United States Census Bureau, it is estimated that 99 000 men will die from prostate cancer in the year 2045 (Chan et al 2004). Besides the health risk, there is also concern about the best way to pay for expensive prostate cancer treatment in the future where an aging population is expected to exhibit high rates of prostate cancer detection (Fowler et al 2000). Despite our best efforts to cure, failure rates for prostate cancer may be as high as 40%–60% in high-risk cases (Tefilli et al 1999).

Epidemiological studies suggest that diets rich in grains, specific vitamins, fruits, and vegetables are associated with lower prostate cancer rates than high fat diets associated with red meat, dairy product intake, and high dose calcium (Cohen et al 2000; Michaud et al 2001; Lamb and Zhang 2005; McCann et al 2005; Walker et al 2005; Wolk 2005). High temperature cooking and/or well-done or charred meat contains heterocyclic amines, nitrosamines, and polycyclic aromatic hydrocarbons that have been shown prospectively to increase prostate cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. (Cross et al 2005) Dairy products and diets with high calcium content have also been found to increase the risk of prostate cancer possibly through an increase in phytanic acid levels which are also elevated in high meat (protein) diets (Mayer 2005; Xu et al 2005). A number of studies have found an association between saturated fat and prostate cancer although the precise mechanisms are not clear (Giovannucci et al 1993; Dagnelio et al 2004; Mydlo 2004). We, therefore, selected a modified Mediterranean diet which includes a high intake of cereals, grains, vegetables, fruits, virgin olive oil, beans, garlic, fresh herbs, and seafood or poultry (white meat) with an avoidance of red meat and dairy products (Trichopoulou et al 2000; Knoops et al 2004).

We know that many prostate cancer patients; up to 73% in one study, will take nutritional supplements on their own and the typical patient averages about three separate supplements daily (Boon et al 2003; Eng et al 2003; Chan, Elkin, et al 2005; Wigul et al 2005). Animal studies, epidemiological data, and other evidence suggests that plant-based dietary supplements providing indoles, isothiocyanates, phenolics, monoterpenes, flavonoids, phytosterols, lignan precursors, lycopenes, and soy proteins as well as zinc, selenium, Vitamin E and various other antioxidants may serve as natural inhibitors of prostate carcinogenesis and growth (Jain et al 1999; Chan, Gann, et al 2005; Meyer et al 2005; Schroder et al 2005; Shukla and Gupta 2005; Sonn et al 2005). The "Peenuts®" product is a standardized, certified, and patented nutritional supplement that contains appropriate levels of these ingredients from plant-based sources (Wheeler 2001). The formula has been shown to suppress and help resolve nonbacterial prostatitis in randomized, placebo-controlled double blinded studies and is readily available commercially (Wheeler and Selah 1997; Wheeler 2001). Reductions in white blood cell count in the expressed prostatic secretions of prostatitis patients were reported at 66%–77% using only this nutritional supplement (Wheeler and Selah 1997).

A number of recent studies have suggested that nutritional therapies alone could possibly lower the aggressiveness of prostate cancer and prevent its progression, but randomized clinical trial data so far is very limited and no prospective studies have yet identified an optimal combination of dietary measures and nutritional supplementation that can effectively control prostate cancer growth.

There are many experts who question whether we are overtreating prostate cancer. The poignant words of the late Willet Whitmore, M.D., may prove most prophetic. To paraphrase, his oft-quoted rhetorical question asks, "Is it possible to cure prostate cancer when it is necessary?" and, "Is it necessary to cure prostate cancer when it is possible?" If we accept that a cure is not always possible or even desirable in some cases due to complications, surgical risks, side effects, morbidity, cost, and patient choice, this leads us to the next logical question, "Is it possible to significantly suppress or slow prostate cancer growth for prolonged periods using only nutritional and dietary measures?" The goal of this study was to attempt to begin to answer this important question by prospectively treating prostate cancer patients exclusively with conservative measures including optimal dietary modification and standardized complex nutritional supplementation to determine the feasibility and effectiveness of such an approach as a possible alternative in prostate cancer treatment.

Methods and materials

Between 1998 and 2004, 23 men (mean age: 63 years) with biopsy proven prostate cancer, who had declined attempts at curative cancer treatment and hormonal therapy, were given full informed consent and offered the opportunity to

try a strictly dietary and nutritionally oriented conservative protocol. The diet used was a Modified Mediterranean Diet (Prostate Diet) while a patented prostatitis formula (Peenuts®) was the nutritional supplement common to all patients. By study design, none of the patients had ever been exposed to antiandrogen therapy, a luteinizing hormone-releasing hormone (LHRH) analogue, LHRH antagonist, or definitive therapy with surgery, radiation, or cryosurgery. All men were followed at varying time intervals with a PSA (prostate specific antigen) blood test, while many of the men were also followed with the International Prostate Symptom Score (IPSS) index and the expressed prostatic secretion (EPS) examinations. With the exception of two men with Gleason 6/7 components, three men with Gleason 5/6 components, and one male with a Gleason 7 pattern, all men exhibited either a Gleason 5 (n = 6) or a Gleason 6 (n = 11) pathological pattern. All men were clinically diagnosed as T1c (n = 15), T2a (n = 2), T2b (n = 2), or T2c (n = 4). Interestingly, all of the men who met the entry criteria outlined above except one, enthusiastically chose to treat their disease through a dietary and nutritional supplement protocol represented by the term Chronic Disease Management (CDM) rather than undergo definitive therapy. The one male who initially qualified dropped out after 7 months, opting for a radical prostatectomy. CDM therapy is a unique cancer concept, but not dissimilar to the conservative holistic treatment of diabetes, hypertension, or arthritis whereby patients learn to live with the disease based on lifestyle changes consistent with improved diet, nutritional supplementation, stress reduction, and exercise.

While the PSA level is a recognized marker of disease activity, it is noted that PSA levels may rise based on any combination of prostatitis (nonbacterial inflammation in ≥95% of cases), BPH (benign prostatic hyperplasia), and/or prostate cancer. The IPSS index is a recognized marker associated primarily with BPH and prostatitis, while the EPS represents the diagnostic biological marker for prostatitis. All men were evaluated at varying intervals of surveillance ranging from 13 months to 84 months (mean: 38.5 months). Three study subjects had a slight increase in their PSA levels of 0.3 ng/ml, 0.7 ng/ml, and 0.9 ng/ml at 14 months, 42 months, and 34 months, respectively. Excluding these three patients with a small rise in PSA, the remaining 20 patients (87%) decreased their PSA levels by an average of 58% during the study period.

Statistical analysis

A performance analysis of these 23 patients relevant to any change in PSA noted statistical significance using the null hypothesis, t-test, and Wilcoxon analyses. There was a significant decrease in PSA levels (ng/ml) after treatment with dietary modification and the specific herbal supplement taken at 2 capsules daily. The p-value ($T \leq t$) one-tailed t-test is 0.000068.

The null hypothesis can be postulated from the population of 23 patients. The first observation, u_1, is the initial PSA value taken. The second observation, u_2, is the follow-up PSA taken after treatment with the herbal supplement and dietary change. H0: $u_1 - u_2 = 0$. The null hypothesis postulates that the mean value of the difference is zero. There will be no significant difference in PSA levels after herbal supplementation and dietary change.

In the alternative hypothesis, the mean is different using the observed values; therefore, a two- tailed test is utilized (Table 1).

Statistical assessment

There was a significant decrease in PSA levels (ng/ml) after treatment with dietary encouragement and herbal supplementation, 2 capsules daily. Therefore we do not accept the null hypothesis that the mean difference is zero. These nutritional variables had a significant effect in reducing PSA levels in this subject group. An additional non-parametric test was calculated. The results of the Wilcoxon matched-pairs signed-ranks test are as follows: W+ = 269.50, W– = 6.50, n = 23, p ≤ 6.769005 (Table 2, 3).

Results

All men within an age range of 43–74 years with a diagnosis of prostate cancer (Gleason Score: 5, 5/6, 6, 6/7, 7) who declined standard curative and hormonal therapy were offered an opportunity to participate in a conservative quality of life

Table 1 T-test: Paired two sample for means. Alpha significance level = 0.05

	Initial PSA	Follow-up PSA
Mean	6.83	3.36
Variance	8.76	6.34
Observations	23	23
Pearson correlation	0.43	
Hypothesized mean difference	0	
Df	22	
t stat	5.65	
p (T ≤ t) one-tail	0.000006	
t critical one-tail	1.717144	
P (T ≤ t) two-tail	0.000011	
t critical two-tail	2.073875	

Abbreviations: Df, degrees of freedom; PSA, prostate specific antigen.

Table 2 T-test: paired two sample for means: 5-alpha reductase inhibitors

	Dx. PSA (ng/ml)	Follow up PSA
Mean	6.38461538	2.6153846
Variance	10.2680769	1.1214103
Observations	13	13
Pearson correlation	–0.05984581	
Hypothesized mean difference	0	
Df	12	
t Stat	3.95697795	
p (T ≤ t) one-tail	0.00095184	
t Critical one-tail	1.78228674	
P (T ≤ t) two-tail	0.00190367	
t Critical two-tail	2.17881279	

Note: The p value is statistically significant at 0.0019.
Abbreviations: Df, degrees of freedom; Dx, diagnosis; PSA, prostate specific antigen.

protecting study with the understanding that diet and nutrition could play a significant role in disease proliferation or control. With the exception of the Gleason Score (excluding men with a primary Gleason Score of 8, 9, or 10) as a qualifying category of prostate cancer, there was no bias inherent in the entrance process. Twenty three men qualified for study evaluation using the PSA levels from the date of diagnosis (biopsy date) or the initial clinic appointment date (whichever was higher) as the reference PSA value for the starting point for data collection. Twenty of 23 men experienced a positive response (decrease in PSA levels) relevant to the conservative therapy while 3 men noted a mild increase in their PSA values. Specifically, 87% of men (n = 20) noted a 58% reduction (range of improvement: 13%–90%) in PSA levels over an average of 38.5 months (range: 13–84 months). Using a mean PSA starting point of 6.8 ng/ml, 87% of men in the study experienced a mean reduction in PSA of 3.93 ng/ml (range: 0.9–12.5 ng/ml) over the identified time frame, while the median reduction was 3.45 ng/ml. The three men, who experienced a mild elevation in PSA, noted an increase of 0.3 ng/ml, 0.7 ng/ml, and 0.9 ng/ml over 14 months, 42 months, and 34 months, respectively. Overall, the effectiveness of CDM therapy to suppress prostate cancer was 87% using the PSA level as the disease activity marker.

Table 3 T-test: paired two sample for means: non-5-alpha reductase inhibitors

	Dx. PSA	Follow-up PSA
Mean	7.06	4.64
Variance	8.987111111	8.707111111
Observations	10	10
Pearson correlation	0.891877977	
Hypothesized mean difference	0	
Df	9	
t Stat	5.529914009	
p (T ≤ t) one-tail	0.000182887	
t critical one-tail	1.833113856	
p (T ≤ t) two-tail	0.000365774	
t critical two-tail	2.262158887	

Note: The p value is statistically significant at 0.00037.
Abbreviations: Df, degrees of freedom; Dx, diagnosis; PSA, prostate specific antigen.

A urinary assessment with a voiding symptom score (IPSS index) and prostatitis evaluation utilizing the EPS examination was conducted at the time of baseline (initial visit) and follow up evaluations on the majority of the participants. Fifteen men completed an initial and secondary IPSS index while 14 men had undergone an initial and secondary EPS. All men reduced their voiding symptom score with an average 4.9 points (range: 3–11), while noting an average starting score of 9.1 points (range: 2.5–19.5 with a median of 8.5). The mean percentage reduction in IPSS index was 61% (range: 20%–100% with a median of 55%). Relevant to the EPS, an average starting point of 283 white blood cells (WBCs) per high-powered field (HPF) (400X) demonstrated an average decrease to 65 WBCs/HPF. To state further, a mean reduction was noted in the prostatitis marker of 218 white blood cells (range: 70–495) with a mean percentage improvement of 77.5% (range: 33%–99% with a median of 82%). The reduced number of white blood cells on the EPS examinations as well as the improvement in urinary symptoms as documented by the average reductions in IPSS index scores in this group of men treated with nutritional means alone was statistically significant.

Study analysis and discussion

The possibility of treating prostate cancer conservatively has always been intriguing to the patient and a concern for the clinician. Previous studies have commonly grouped Gleason 7 scores with Gleason 5 and 6 scores within the designation of moderately well differentiated cancers. Ostensibly, this would give patients with Gleason 7 scores improved odds for cure while decreasing the chance for success in patients with Gleason 5 and 6 scores. This assumes the higher the Gleason score, the lower the chance for cure (Tefilli et al 1999; Nelson et al 2002). Increasing evidence through analyses now suggests that Gleason 7 prostate cancer responds better than a Gleason 8–10 but not as well as a Gleason 5 or 6 (Tefilli et al 1999). Additionally, it is believed that Gleason scores of 5–7 may comprise almost 90% of all cancers encountered as 35%–62% of men in most study groups analyzed are identified in the Gleason 6 category (Tefilli et al 1999).

Qualification for this study included men with the diagnosis of prostate cancer who had not been exposed previously to antiandrogen therapy, LHRH therapy, or any other definitive process of prostate cancer manipulation. Of the 23 patients evaluated, 11 men were diagnosed with a Gleason 6 score, 6 men had a Gleason 5 score, 3 men had a Gleason 5–6 score, 2 men were noted with a Gleason 6–7 score, while one man had a Gleason 7 pattern. The clinical stage assessment noted 15 men with a T1c, 4 men with a T2c, 2 men with a T2b, and 2 men with a T2a stage classification. Pathologically, the biopsy diagnosis ranged from T1a–T2c (Table 4). While the number of biopsy cores positive for cancer and the percentage of cancer per core varied widely, the percentage of cores positive for cancer (identified at the biopsy procedure) ranged from 12.5%–73% (mean: 33%; median 20%) associated with a range of biopsy samples from 2–18. This suggests the presence of significant disease in the study group.

In a unique study, Dean Ornish and colleagues at the University of California-San Francisco evaluated the ability of the Vegan Diet (n = 44) to alter the PSA in a comparative analysis with a nonrestrictive diet (n = 43) in men documented with a Gleason 6 prostate cancer over a one year time period (Omish et al 2005). All of the men in this study, as in ours, had declined definitive curative treatment and hormonal therapy. While the merits of the Vegan Diet cannot be disputed as a benefit in heart disease prevention, it was less clear what effect this diet would have on men with known prostate cancer. An average decrease in PSA of 0.25 ng/ml (4%) identified in the Vegan group was statistically significant when evaluated in concert with a 0.38 ng/ml (6%) rise in the placebo group. While statistically significant, the difference was nonetheless modest at one year. This study result does not suggest a lack of benefit to the Vegan Diet, but rather demonstrates that the impact of diet alone on prostate cancer may be modest.

In our prospective study, we evaluated the benefit of a modified Mediterranean diet on known prostate cancer patients with Gleason scores of 5–7. The Mediterranean diet is recognized worldwide for its health benefits systemically but more specifically its promotion of cardiovascular health and cancer avoidance (colorectal, breast, pancreas, prostate, and endometrial) properties (Trichopoulou et al 2000; Knoops et al 2004; Giugliano and Esposito 2005; Williams and Hord 2005). By design, men were asked to avoid red meat and dairy products including eggs in an effort to decrease saturated fat. It is commonly recognized that animal fat and dairy fat may play a role in prostate cancer proliferation (Giovannucci et al 1993; Cohen et al 2000; Michaud et al 2001; Margolis and Carter 2002; Dagnello et al 2004; Mydlo 2004; Cross et al 2005; Lamb and Zhang 2005; Mayer et al 2005; McCann et al 2005; Walker et al 2005; Wolk 2005; Xu et al 2005). Unlike the Ornish cohort, men did not use soy in their diets.

Table 4 Chronic disease management protocol noting PSA response to 5–alpha reductase inhibitors (5-ARIs) versus non-5-ARIs (August 2005)

5-ARIs					Non-5-ARIs				
Dx. PSA (ng/ml)	**Gleason Score**	**Follow up PSA**	**Surveillance Months**	**Percent change**	**Dx. PSA (ng/ml)**	**Gleason Score**	**Follow up PSA**	**Surveillance Months**	**Percent change**
8.5	5	3.1	72	64%	7.0	5	2.4	62	66%
5.4	6	2.1	41	61%	11.7	5/6	5.8	60	50%
2.1	5	2.8	42	+33%	4.7	6	1.7	72	64%
7.3	5/6	4.5	40	38%	6.9	6	5.1	19	26%
3.2	6	2.0	21	38%	6.9	6	6.0	38	13%
4.4	6/7	1.7	39	61%	9.1	6	5.5	58	40%
6.8	5	1.7	49	75%	3.0	5	0.8	24	73%
8.4	6	1.8	18	79%	6.2	5	4.1	84	34%
4.4	6/7	4.7	14	+7%	11.4	6	12.3	34	+8%
14.4	6	1.5	29	90%	6.6	6	1.8	24	73%
4.1	6	1.6	15	61					
6.1	5/6	1.3	13	79					
8.6	7	2.9	17	66%					
Average starting PSA 6.44 ng/ml	5.9	2.44	32 Months	52%	Average starting PSA 7.35 ng/ml	5.65	4.55	48 Months	43.1%

Notes: Average reduction in PSA with 5-ARIs = 4.0 ng/ml; average reduction in PSA with non-5-ARIs = 2.8 ng/ml.

Abbreviations: ARIs, alpha-reductase inhibitors; Dx, diagnosis; PSA, prostate specific antigen.

Fresh fruits and cruciferous vegetables belonging to the brassica classification were highlighted while the oil of choice was virgin olive oil.

Beyond the modified Mediterranean Diet, our study group used a complex nutritional supplement called Peenuts® that was originally developed to treat prostatitis. This formula represents a unique, synergistic blend of vitamins, minerals, amino acids, and herbs. These ingredients have been shown individually to affect cellular oxidation, inflammation, and immune function, while less clearly offering additional potential benefits from beta-sitosterols (PDR 2000; MSKEB 2004). While using this formula, previous clinical investigations have shown an improvement in the EPS and voiding symptoms (Wheeler and Selah 1997). The EPS is the recognized diagnostic marker for prostatitis as shown through the historic work of Stamey, Meares, and others (Blacklock and Beavis 1974; Anderson and Fair 1976; Drach et al 1978; Anderson and Weller 1979; Schaeffer et al 1981), while voiding symptoms are common to the diagnosis of benign prostatic hyperplasia and prostatitis.

The concept of looking at prostatitis within this study group was prompted by previous research from the American Association of Cancer Research (AACR) that supports a role for prostatitis in the evolution of prostate cancer (AACR 2001; Nelson et al 2004; Smith and Missailidis 2004). It is postulated that the cellular oxidative stress associated with a chronic inflammatory process leads to proliferative inflammatory atrophy with subsequent evolution of free radicals through oxidative change eventually resulting in DNA alteration (cellular mutation), prostatic intra-epithelial neoplasia (PIN), and cancer (AACR 2001; Nelson et al 2004). While it is beyond the scope of this article to review these findings in greater depth, it is well known that the process of inflammation is commonly associated with organ specific cancers including but not limited to cancer of the esophagus, colon, stomach, liver, lung, and cervix (Balkwill and Mantovani 2001; Coussens and Werb 2002; Smith and Missailidis 2004).

Within our study group, the mean PSA at the time of diagnosis was 6.8 ng/ml (range: 2.1–14.4 ng/ml). A statistically significant reduction in mean PSA of 3.4 ng/ml was validated using the t-test, Wilcoxon analysis and the null hypothesis (Table 5). The mean percentage reduction in PSA was 50% while the likelihood for organ confinement in this group was 66% referencing the Partin Prediction tables (Partin et al 1997, 2001).

While the topic of prostatitis and its role in prostate cancer evolution is likely to remain controversial for the immediate future, the topic's relevance may be best left for the healthcare provider and the patient to decide. Based on an average percent reduction in the WBCs (a universal marker for inflammation) of 77.5% associated with the EPS, there appears to be sufficient clinical indication to support the addition of a scientifically validated prostatitis therapy to any long-term prostate cancer management protocol. The relative failure of the Vegan diet in the Ornish study to significantly suppress prostate cancer (based on PSA analysis) supports this hypothesis.

Additionally, it is not unreasonable to suggest the noted reduction in PSA in our study is based mainly on the improvement in prostatitis as it is well known that prostatitis is a common cause of PSA elevations. However, the long average duration of the reduction in PSA levels at over 3 years in patients with known prostate cancer receiving no other therapy would suggest that the treatment is acting directly on the prostate cancer. Only further study will be able to determine if this conclusion is accurate. At the very least, we can say that the nutritional component complements the diet and may well enhance the durability of response seen in the study patients.

There is a clear indication that the nutritional treatment evaluated had an impact on voiding symptoms, as there was a mean percentage reduction in the IPSS index of 61%. This is consistent with findings from a previously performed randomized, double blind, placebo controlled study (Wheeler and Selah 1997). This response exceeds that of any prostate or prostatitis nutritional formula such as saw palmetto described in the world medical literature suggesting a synergistic effect from the particular blend of nutrients selected (Kaplan et al 2004).

One gentleman aged 54, who had initially qualified for the study, decided on a radical prostatectomy despite performing quite well at 7 months. Importantly, the delay in surgery had no adverse effect on the outcome, as his PSA was 0.0 ng/ml, 1 year post-prostatectomy. While further research could evaluate the potential benefit of this protocol to any ultimate outcome, the delay in definitive treatment allowed for improved awareness and decision making on the part of the patient and his family. Alternatively, research may demonstrate the use of the Peenuts® formula or similarly validated supplements to be a reasonable first step in avoiding additional biopsies in patients where prostatitis is present.

While the use of the modified Mediterranean diet and a prostate nutritional supplement has been shown to be effective, additional ingredients and/or products may be added to enhance the collective benefit in the prostate cancer disease suppression process. Beyond the modified Mediterranean

Table 5 Patient data for prospective prostate cancer study

Age	Initial PSA PSA	Follow up decrease	% PSA disease	Time with score	Gleason stage	Clinical stage	Biopsy	IPSS index change	IPSS change	EPS	EPS
61	8.5 ng/ml	3.1 ng/ml	64%	72 months	5 (3+2)	T2c	T2c	5.5–2.5 = 3	55%	256–113	56%
68	7.0 ng/ml	2.4 ng/ml	66%	62 months	5 (3+2)	T1c	T2a	19.5–8.5 = 11	56%	85–15	82%
43	5.4 ng/ml	2.1 ng/ml	61%	41 months	6 (3+3)	T1c	T2a	4–0 = 0	100%	325–60	82%
65	11.7 ng/ml	5.8 ng/ml	50%	60 months	5(3+2)/6(3+3)	T1c	T2b				
64	4.7 ng/ml	1.7 ng/ml	64%	72 months	6 (3+3)	T1c	T2a				
55	2.1 ng/ml	2.8 ng/ml	+33%	42 months	5 (3+2)	T2c	T2c	6.5–2 = 4.5	69%	350–158	55%
56	7.3 ng/ml	4.5 ng/ml	38%	40 months	5(2+3)/6(3+3)	T2a	T2b	10.5–6 = 4.5	43%	TNTC–5	99%
70	6.9 ng/ml	5.1 ng/ml	26%	19 months	6 (3+3)	T2c	T2a	11.5–7.5 = 4	35%	268–17	94%
68	6.9 ng/ml	6.0 ng/ml	13%	38 months	6 (3+3)	T1c	T2a	4-0 = 0	100%		
56	9.1 ng/ml	5.5 ng/ml	40%	58 months	6 (3+3)	T1c	T2a	11–7 = 4	36%	375–150	60%
61	3.0 ng/ml	0.8 ng/ml	73%	24 months	5 (3+2)	T1c	T2a				
48	3.2 ng/ml	2.0 ng/ml	38%	21 months	6 (3+3)	T2a	T2b	9.5–2 = 7.5	79%	278–40	86%
69	6.2 ng/ml	4.1 ng/ml	34%	84 months	5 (3+2)	T1c	T1a	15.5–10 = 5.5	35%	205–9	96%
56	4.4 ng/ml	1.7 ng/ml	61%	39 months	6(3+3)/7(3+4)	T2c	T2c	8.5–1.5 = 7	82%	350–30	91%
74	11.4 ng/ml	12.3 ng/ml	+8%	34 months	6 (3+3)	T2b	T2b				
63	6.8 ng/ml	1.7 ng/ml	75%	49 months	5 (3+2)	T1c	T2a	5.5–2.5 = 3	55%	275–70	75%
71	6.6 ng/ml	1.8 ng/ml	73%	24 months	6 (3+3)	T1c	T2c	7.5–6 = 1.5	20%	185–35	81%
64	14.4 ng/ml	1.5 ng/ml	90%	29 months	6 (3+3)	T1c	T2a				
70	8.4 ng/ml	1.8 ng/ml	79%	18 months	6 (3+3)	T1c	T2a				
72	4.4 ng/ml	4.7 ng/ml	+7%	14 months	6(3+3)/7(3+4)	T2b	T2c				
55	4.1 ng/ml	1.6 ng/ml	61%	15 months	6(3+3)	T1c	T2c	2.5–0 = 0	100%	210–10	95%
72	6.1 ng/ml	1.3 ng/ml	79%	13 months	5(3+2)/6(3+3)	T1c	T2c				
71	8.6 ng/ml	2.9 ng/ml	66%	17 months	7(4+3)	T1c	T2a	14.5–7 = 7.5	52	300–200	33%
TOTALS:	**157.2 ng/ml**	**77.2 ng/ml**	**802**	**885**							

Note: Gleason score: 2–10 (Primary Cancer Grade + Secondary Cancer Grade) with 2 being the most favorable and 10 being the worst.
Abbreviations: EPS, expressed prostatic secretion (an indication of prostate inflammation); IPSS, International Prostate Symptom Score; PSA, prostate specific antigen; TNTC, too numerous to count.

diet and the Peenuts® nutritional formula that were used by all patients, 17 patients used an active form of vitamin D, 13 patients used an anticholesterolemic agent, 14 patients used omega-3 fatty acids, 13 patients used a 5-alpha reductase inhibitor (5-ARIs), 7 patients used a COX II inhibitor, and 4 men used an alpha-blocker. When the men using 5-ARIs were studied versus the men who didn't use them, there was a 52% reduction in PSA in the 5-ARIs group (n = 13) over 32 months versus a 43% reduction in the cohort not on 5-ARIs (n = 10) over 48 months. This suggests a relatively insignificant benefit in PSA reduction relevant to the men on the 5-ARIs at this point in the study. Interestingly, when the nutritional supplement formula was evaluated alone (n = 4), a reduction in mean PSA of 53.8% over 41.3 months of surveillance was noted. While this finding is potentially quite significant, it would be premature to draw any conclusions from such a small sampling size and a larger study with additional patients would need to be completed before the issue can be properly addressed.

Conclusions

Prostate cancer is recognized as the number one male cancer health risk with a new case diagnosed every 3 minutes. With baby boomers aging and healthcare costs rising (Gelman 2004), an opportunity to examine novel concepts for the care of patients diagnosed with prostate cancer could not be more relevant. When a radical prostatectomy is successfully performed for a cure, consideration should be given to the potential average benefit of adding 3 years, 1.5 years, and 0.4 years to the life of a typical man in his 50s, 60s, or 70s, respectively. When this benefit is weighed against the possibility of failure to cure and the associated morbidity, pain, surgical risks, complications, side effects, and costs, an effective dietary and nutritional protocol may present a reasonable alternative (Coley et al 1997).

When all of these factors are considered in our aging population together with the risks of a significant decrease in the quality of life even in successful cases of definitive, curative therapy, a conservative approach may be welcomed as a viable first choice in Gleason 5 and 6 prostate cancer patients by Governmental agencies such as Medicare, the healthcare insurance industry, and patients alike. Critical to research regarding the concept of living with the disease is to locate and allocate funding to study this protocol and similar programs in greater depth with additional patients followed over a longer period of time. This study has perhaps provided the first step in our improved understanding of the concept of nutritional therapy of prostate cancer. Beyond the issue of prostate cancer treatment is the potential role of prevention. Ultimately through this research effort and that of others, the landscape of prostate cancer treatment will become better defined.

Addendum

Description of the patented prostatitis formula

Peenuts® is a standardized formula for prostate health readily available around the world. The formula is a proprietary blend of vitamins, minerals, amino acids, and beta sitosterols. The following ingredients make up this formula:

- Vitamins–C, B6, E
- Minerals–zinc, selenium,
- Herbs–Saw palmetto, *Pygeum africanum*, stinging nettle, pumpkin seed, *Echinacea purpurea*, garlic, ginkgo biloba
- Amino acids–L-glycine, L-alanine, L-glutamic acid.

Modified Mediterranean Diet

The Modified Mediterranean Diet encompasses all of the traditional components of a standard Mediterranean Diet including fresh fruits and vegetables, olive oil, Omega 3 fatty acids, fish, tomato and tomato-related products, and red wine. The modification to this diet comes with a limitation of pasta as well as an avoidance of red meat and dairy fat associated with a fatty acid called Arachidonic acid found in the saturated fats of these food items. Based on references sited in the bibliography, Arachidonic acid has been shown to cause prostate cancer to grow aggressively in vitro.

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