

Short Communication

Comparison of Low-Carbohydrate Vs. A Low-Fat Diet on Prostate Cancer Biomarkers

John C. Mavropoulos¹, Adele H. Hite², Lauren E. Howard^{3,4}, Adriana C. Vidal^{3,5}, Lionel L. Banez⁵, Daniel M. Levine⁶, William J. Aronson^{7,8}, William S. Yancy^{2,9}, Eric C. Westman² and Stephen J. Freedland^{3,5,10*}

¹Department of Dermatology, Johns Hopkins University, USA

²Department of Medicine, Duke University Medical Center, USA

³Department of Surgery, Durham VA Medical Center, USA

⁴Department of Biostatistics and Bioinformatics, Duke University School of Medicine, USA

⁵Department of Surgery, Division of Urology, Duke University School of Medicine, USA

⁶Clinical Research Laboratory, The Rogosin Institute, Cornell University, USA

⁷Department of Surgery, Greater Los Angeles VA Medical Center, USA

⁸Department of Urology, UCLA School of Medicine, USA

⁹Center for Health Services Research in Primary Care, USA

¹⁰Department of Pathology, Duke University School of Medicine, USA

Corresponding author

Stephen J. Freedland, 475 MSRB-I, Research Dr., Duke University, Durham NC 27710, USA, Tel: 1-919-668-5946;

Fax: 1-919-668-7093; E-mail: steve.freedland@duke.edu

Submitted: 14 July 2014

Accepted: 18 October 2014

Published: 20 October 2014

ISSN: 2333-7125

Copyright

© 2015 Freedland et al.

OPEN ACCESS

Keywords

- Low-carbohydrate diet
- PSA
- Prostate cancer

Abstract

Low-carbohydrate diets slow prostate cancer (PC) growth in mice, but PC-safety is questioned due to high-fat content. In this exploratory, ancillary and hypothesis-generating study, we compared sera from PC-free men in a randomized trial of low-fat vs. low-carbohydrate diets for weight loss for prostate-specific antigen (PSA) effects and in vitro PC growth. Baseline and week-24 serum were applied to LAPC-4 human PC cells and cell growth was measured (n=21), leaving minimal week-24 serum leftover. PSA was measured using remaining serum from baseline and week-16 (n=15). Low-carbohydrate diet resulted in more weight loss (median 27.1 vs. 9.4lbs, rank-sum p=0.10), although differences were not statistically significant. At week-16, median PSA was 0.69 ng/ml (IQR 0.50-0.94), with no differences between groups (rank-sum p=0.62). There was no correlation between weight loss and PSA change (Spearman r=0.05, p=0.87). Using baseline serum as reference, week-16 serum stimulated cell proliferation was identical between arms (rank-sum p=0.66). Greater weight loss correlated with decreased cell growth (r=-0.50, p=0.03). A low-carbohydrate diet resulted in greater weight loss than low-fat, but no difference in PSA. Although in vitro PC cell growth was unaffected by diet, cell growth was inhibited by weight loss. Low-carbohydrate diets may lead to greater weight loss and weight loss may inhibit PC growth. Prospective trials in a larger cohort are underway.

ABBREVIATIONS

PC: Prostate Cancer; PSA: Prostate-Specific Antigen; BMI: Body Mass Index; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; Low-Carb: Low Carbohydrate

INTRODUCTION

Prostate cancer is an epidemic in Western society whereas Asian nations have relatively low incidence and mortality rates [1]. One factor postulated to explain this disparity is diet, which

differs markedly between these two populations [2]. To date, studies of prostate cancer and diet have focused mostly on fat intake. Indeed, multiple studies in both animals [3,4] and humans [5-7] suggest that increased dietary fat promotes prostate cancer development and growth. Given that numerous epidemiological studies have linked diets high in fat and processed meat with cancer growth, the American Cancer Society recommends a diet low in fat and meat intake, and rich in plant carbohydrates and fiber during and after cancer treatment [8].

In light of these dietary recommendations, it may be suspected that diets high in fat, protein and refined carbohydrates would stimulate tumor growth and thus should be avoided in cancer survivors. Whereas diets rich in plant-based foods have shown to have a protective effect on prostate cancer [9], recent evidence from a randomized trial found minimal effect of low-fat diets on asymptomatic, hormonally naïve prostate cancer patients [10]. Moreover, even though results from randomized trials suggest a low-carbohydrate diet may result in weight loss that is similar to or better than more traditional low-fat diets [11-14]. There are no randomized trials studying the effect of low-carbohydrate diets on prostate cancer prognosis. Given that carbohydrate restriction often results in overall energy restriction and that energy restriction results in both loss of overall body weight and slower tumor growth [15], carbohydrate restriction may be a safe diet for men with prostate cancer [16]. Indeed, animal data from our laboratory and others suggest carbohydrate restricted diets may slow tumor growth in tumor-bearing mice [17,18]. In addition, excessive consumption of refined carbohydrates is strongly associated with the production of pro-inflammatory molecules [19]. We previously found that higher levels of circulating inflammatory markers correlate with higher levels of PSA among healthy men [20]. As such, this might suggest that carbohydrate restriction would lower inflammation, which may lower PSA levels, even in healthy men. Alternatively, if carbohydrate restriction led to high intake of fat, which can also promote inflammation, then a low-carbohydrate diet may promote inflammation thereby raising PSA levels. However, to date, there are no published clinical data on the effects of carbohydrate restriction on prostate biology or prostate biomarkers in humans.

Accordingly, in this study, we conducted a comparative analysis of serum from obese men without cancer who participated in a 24-week randomized trial comparing a low-carbohydrate to a low-fat diet for weight loss. In particular, we assessed levels of prostate specific antigen (PSA), a commonly used prostate cancer biomarker, and the effects of serum to stimulate *in vitro* prostate cancer growth. We hypothesized a low-carbohydrate diet to be anti-inflammatory and to correlate with lower PSA levels. In secondary analyses, we tested the hypothesis that weight loss reduces *in vitro* PC growth.

MATERIALS AND METHODS

Study population and sample collection

Subjects for the current study were a subset of men enrolled in a previously described prospective randomized 24-week trial of a low-carbohydrate versus a low-fat diet with a primary outcome of weight loss. In brief, 120 subjects were enrolled in the original study. Entry criteria included a BMI greater than 30 kg/m² and elevated lipid levels. Subjects were randomly assigned to either a low-carbohydrate or low-fat diet.

Diet intervention description

The low-carbohydrate group was instructed to consume less than 20 grams of carbohydrate per day and could increase carbohydrate intake modestly as the weight loss goal was approached; energy intake was unrestricted. The low-fat group was instructed to consume less than 30% of daily energy from

fat, less than 10% of daily energy from saturated fat, and 500 kcal less than the calculated maintenance energy intake. All participants were encouraged to exercise and asked to attend group meetings. Group meetings with study investigators were held twice per month for the first three months and then once per month for the final three months. Overall, only one subject dropped out of the study after randomization but prior to the institution of diet. Of the remaining 119 study subjects, 28 (24%) were male (13 in the low-fat group and 15 in the low-carb group).

Fasting serum samples were obtained at baseline and again at 8, 16, and 24 weeks and were frozen at -80°C for subsequent analysis. Banked serum from baseline and week 24 was initially used for the *in vitro* bioassay (see below). Of the remaining serum, 8 men had no serum samples available at any time point for PSA measurements. Of the remaining 20 men, only four men had serum remaining from the week 24 time point, and thus, the 16 week time point was regarded as the end of this study for the PSA analysis. Of the 20 men with serum available for PSA, three subjects did not have baseline serum available and two did not have serum available at week 16. Thus, the final cohort for the PSA analyses included the 15 men with both baseline and week 16 serum available for evaluation.

Serum PSA analysis

Serum levels of fasting total and free PSA were measured via Immulite 2000 Advanced Immunoassay chemiluminescent enzyme-immunoassay (Diagnostic Products Corp., Los Angeles, CA) using the Randox tumor marker panel (Diagnostic Products Corp., Los Angeles, CA). Frozen serum samples were thawed, homogenized, and analyzed on a fully automated analyzer at room temperature. The free PSA assay has a sensitivity of 0.02ng/ml and a coefficient of variation for intra- and inter-assay precision of 8.7% and 8.5%, respectively. The total PSA assay has a sensitivity of 0.045ng/ml and a coefficient of variation for intra- and inter-assay precision of 8.7% and 8.4%, respectively.

In vitro bioassay

A total of 21 men (13 low-carbohydrate and 8 low-fat) had frozen serum from both baseline and 24 weeks available for *in vitro* stimulated mitogenicity. The effect of fasting serum on LAPC-4 cell proliferation was examined as previously described [3,21]. In brief, LAPC-4 cells were plated *in vitro* with Iscove's modified medium and 10% fetal bovine serum (FBS) under standard culture conditions. After 24 hours, fresh media was added and supplemented with either 10% FBS (control) or 10% patient serum. Following another 48 hours of incubation, cell viability was measured using the CellTiter 96AQ Assay (Promega Corporation, Madison, WI). This method has been shown to correlate (<5% difference) with 3H-thymidine incorporation and was used to determine the number of viable cells in each well. Serum samples collected at baseline and week 24 for each study subject were analyzed in triplicate for their pre- and post-intervention ability to stimulate cellular proliferation.

Statistical analysis

Comparison between the groups was performed using the rank-sum test for continuous variables. The ratio of the post-intervention vs. pre-intervention cell proliferation was compared

between dietary arms using rank-sum test and as a function of weight loss across both arms using a Spearman rank correlation. The ratio of the post-intervention vs. pre-intervention PSA was compared between dietary arms using rank-sum test. Thus, all endpoints measured at the end of the study were compared to pre-intervention levels. All statistical analyses were performed using STATA 11.0 (Stata Corp., College Station, TX) with an $\alpha=0.05$ cut-off for statistical significance. No corrections were conducted for multiple comparisons.

RESULTS AND DISCUSSION

Subjects

Of the 28 men who completed the weight loss study, serum for PSA analysis at both baseline and 16 weeks was available from 15 subjects, 10 on the low-carbohydrate arm and 5 on the low-fat arm. There were no significant differences in baseline variables (age, body weight, BMI, height, and serum lipids) between the groups (Table 1).

Weight loss

Among the 15 study subjects, median weight loss from baseline to 16 weeks was 25.4 lbs (IQR 18.2 to 31.0 lbs). Men on the low-carbohydrate diet lost more weight than men on the low-fat diet, however this did not reach statistical significance (median weight loss of 27.1 lbs. vs. 9.4 lbs; rank-sum, $p=0.10$).

PSA

The median pre-intervention serum PSA value was 0.76 ng/ml (IQR 0.45 to 1.01 ng/ml), with no significant differences between groups ($p=0.50$; Table 2). At the completion of the study,

the median serum PSA value was 0.69 ng/ml (IQR 0.50 to 0.94 ng/ml), with no significant differences between groups ($p=0.62$). Similarly, percent free PSA did not differ between dietary arms either at baseline ($p=0.71$) or at the completion of the study ($p=0.54$). A total of 10 subjects (67%) had a decline in serum PSA. In particular, 7 out of 10 low-carbohydrate diet subjects (70%) and 2 out of 5 low-fat diet subjects (40%) had decreased PSA levels (chi-squared, $p=0.70$). Using the post to pre-intervention PSA ratio, there were no differences between arms ($p=0.59$). There was no significant correlation between weight loss and change in serum PSA (Spearman $r=0.05$, $p=0.87$).

In vitro cell proliferation

Frozen baseline and 24-week serum were available for 21 men to measure serum stimulated in vitro cell proliferation. Characteristics for these 21 men were similar to the 15 men used in the PSA analysis with no significance differences in any baseline characteristics between the arms. Using the baseline assay as the reference, serum stimulated cell proliferation was similar for men on the low-carbohydrate (median 105%; IQR 94-120%) and men on the low-fat diets (median 105%; IQR 101-145%; rank-sum, $p=0.66$, Figure 1). There was a significant correlation between greater weight loss and decreased cell stimulation ($r=-0.50$, $p=0.03$, Figure 2).

While it is thought that diet plays a role in modulating prostate cancer growth, it remains unclear whether energy restriction as a whole, and/or dietary macronutrient distribution influence this process. Thus, defining which nutritional components -i.e. fat, protein, carbohydrates, or a combination thereof, are critical mediators is key. Historically, dietary fat has been associated

Table 1: Baseline characteristics of patients randomized to the two diet arms.

	Low-Carbohydrate Diet n=10	Low-Fat Diet n=5	P-value
Age (years)	43 (36-53)	52 (45-54)	0.20
BMI (kg/m ²)	33.5 (30.7-35.1)	37.4 (35.7-39.6)	0.18
Height (inches)	71 (70-72)	70 (68-71)	0.36
Weight (pounds)	243.9 (219.8-254.4)	248.6 (234.4-291.2)	0.46
Total cholesterol (mg/dL)	248 (241-273)	244 (223-244)	0.55
Triglycerides (mg/dL)	138 (125-190)	173 (173-209)	0.35
LDL (mg/dL)	170 (162-206)	156 (145-160)	0.26
HDL (mg/dL)	45 (43-46)	44 (40-46)	0.64

All measures are median (25th percentile-75th percentile); P-values are from rank sum tests

Abbreviations: BMI: Body Mass Index; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein.

Table 2: Changes in PSA and percent free PSA after dietary intervention.

	All patients	Low-Carb Diet	Low-Fat Diet	P-value
PSA (ng/mL)				
Baseline	0.76 (0.45-1.01)	0.77 (0.56-1.08)	0.57 (0.45-0.98)	0.50
End of study	0.69 (0.50-0.94)	0.72 (0.53-1.02)	0.59 (0.50-0.85)	0.62
% Free PSA (ng/mL)				
Baseline	0.13 (0.10-0.21)	0.15 (0.10-0.21)	0.11 (0.10-0.18)	0.71
End of study	0.16 (0.10-0.19)	0.15 (0.10-0.20)	0.16 (0.10-0.17)	0.54

All measures are median (25th percentile-75th percentile) and p-values are from rank sum tests of low-carb vs. low-fat diet arm

Abbreviations: PSA: Prostate-Specific Antigen.

with promoting prostate cancer growth [3-7] but such results were based on diets with simultaneous intake of moderate to high levels of carbohydrate. In contrast, the effect of dietary fat on prostate cancer growth in the setting of minimal carbohydrate intake (i.e. a low-carbohydrate diet) has not been evaluated in humans although recent preclinical studies reveal a very high fat diet that is either very low or completely devoid of carbohydrate reduces prostate tumor growth rates relative to comparison diets [17,18,22]. Nonetheless, it remains unclear whether consumption of a low-carbohydrate diet is advisable to men with prostate cancer.

One method to further explore the relationship between carbohydrate intake and prostate cancer risk is to assess the effects of a low-carbohydrate diet on serum PSA levels in men without prostate cancer. In addition, a comparative analysis of diverse diets in such men would provide insight into whether a particular diet is superior with regard to its effects on the prostate. With this goal in mind, we assessed whether a low-carbohydrate diet was superior to a low-fat diet in terms of inducing favorable changes on prostate cancer biomarkers.

In the present study, we used frozen serum samples collected during a previous prospective clinical trial [13] to assess the effect of a low-carbohydrate versus low-fat diet on serum PSA levels in overweight and obese but otherwise healthy men who were seeking weight loss. Within this subset of men with banked serum available, we found that men on the low-carbohydrate diet lost more weight. Though the difference in weight loss was not statistically significant, our subset findings mirror the results of the full cohort reported previously wherein the low-carbohydrate group did lose significantly more weight [13]. We found no significant differences in baseline or week 16 serum PSA values between men on a low-carbohydrate or low-fat diet. While the clinical relevance of this finding to men with prostate cancer can be debated given that the present analysis was conducted in the context of otherwise healthy men (i.e. non-prostate cancer patients), it is important to note that we found no evidence that a low-carbohydrate diet increased PSA levels; in fact, PSA levels decreased in 70% of the men following the low-carbohydrate diet. Thus, while this certainly does not imply that this diet is "safe" in men with prostate cancer, we found no evidence to suggest any prostate-related danger with this diet when using PSA as a surrogate marker.

To further explore the potential implications of a low-carbohydrate diet for men with prostate cancer, we evaluated the growth stimulatory effects of baseline and week 24 sera on a well-established androgen sensitive human prostate cancer cell line (LAPC-4). We found that relative to baseline stimulation, there was no difference in the stimulation seen from the week 24 sera between men on a low-carbohydrate or low-fat diet. This in vitro bioassay has been used previously and demonstrated to correlate with tumor growth in mice models [3]. Moreover, in human clinical trials, a very low-fat vegan diet along with exercise and meditation among men with prostate cancer has been shown to slow in vitro tumor stimulation relative to men making no dietary changes using an identical bioassay [23]. Thus, the lack of difference between in vitro tumor stimulation of the sera from men on a low-carbohydrate versus a low-fat diet is a pertinent negative finding that we believe also suggests no harm from a low-carbohydrate diet. Interestingly, the amount of weight loss was a significant predictor of the degree of decrease in tumor stimulated growth. Thus, while differences in cultured cell growth in this study were not statistically significant between the dietary arms, the positive correlation between weight loss and decreased serum-stimulated growth of cancer cells suggests that weight loss may potentially have a beneficial role in prostate cancer management [16]. Given that low-carbohydrate diets result in more weight loss than other diets for up to 2 years duration [12], this suggests that these diets, in particular, may have a role in prostate cancer management, although further study is clearly needed to confirm or disprove this claim.

Our study was limited by its small sample size and the reliance on intermediate outcome measures related to prostate cancer biomarkers. Thus, we were not able to directly assess the impact of these diets on prostate cancer risk or prostate cancer biology or progression. Specifically, we did not measure serum inflammatory or hormonal markers, hence mechanistic studies were beyond the scope of this trial. Ultimately, future prospective trials specifically designed to ask these questions are needed to

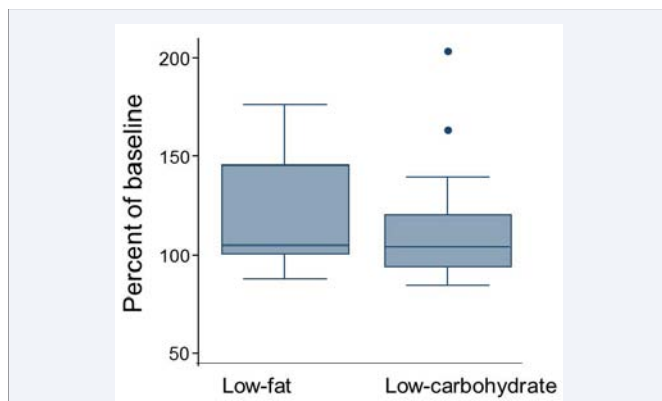


Figure 1 *In vitro* cell proliferation upon stimulation with serum from men on low-fat vs. low-carbohydrate diet.

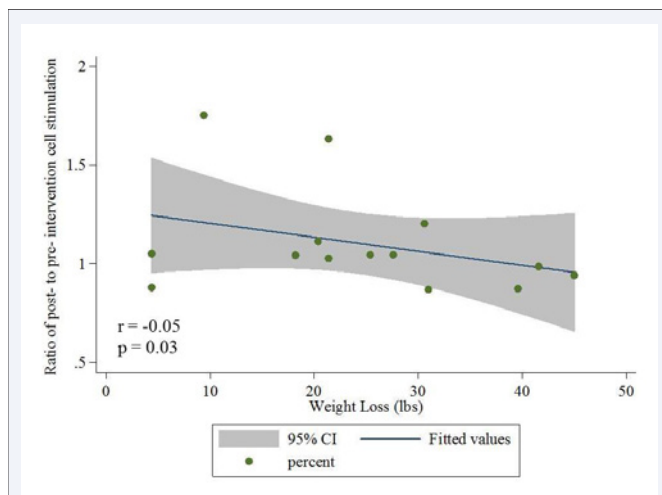


Figure 2 Correlation between weight loss and cell stimulation. Greater weight loss was statistically significantly associated with decreased cell stimulation ($p=0.03$).

determine the safety and perhaps efficacy of a low-carbohydrate diet in prostate cancer management and such trials are underway (clinicaltrials.gov, NCT01763944).

CONCLUSION

In a weight loss trial of men without prostate cancer, a low carbohydrate diet had similar effects on serum PSA levels and serum-stimulated in vitro prostate cancer growth as a low-fat diet. Interestingly, weight loss, regardless of dietary arm, correlated with decreased serum-stimulated in vitro prostate cancer growth. These findings suggest that weight loss, regardless of the diet used to achieve it, may potentially have a beneficial role in prostate cancer management. Finally, given that low-carbohydrate diets may result in more weight loss than other diets for up to 2 years duration, the role of such diets in prostate cancer management merits further investigation.

ACKNOWLEDGEMENTS

This research was supported in part by Grants from the National Institutes of Health K24 CA160653

REFERENCES

1. Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. *Int J Cancer*. 2000; 85: 60-67.
2. Wu K, Hu FB, Willett WC, Giovannucci E. Dietary patterns and risk of prostate cancer in U.S. men. *Cancer Epidemiol Biomarkers Prev*. 2006; 15: 167-171.
3. Ngo TH, Barnard RJ, Cohen P, Freedland S, Tran C, deGregorio F, et al. Effect of isocaloric low-fat diet on human LAPC-4 prostate cancer xenografts in severe combined immunodeficient mice and the insulin-like growth factor axis. *Clin Cancer Res*. 2003; 9: 2734-2743.
4. Wang Y, Corr JG, Thaler HT, Tao Y, Fair WR, Heston WD. Decreased growth of established human prostate LNCaP tumors in nude mice fed a low-fat diet. *J Natl Cancer Inst*. 1995; 87: 1456-1462.
5. Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer MJ. Prospective study of plasma fatty acids and risk of prostate cancer. *J Natl Cancer Inst*. 1994; 86: 281-286.
6. Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CG, et al. A prospective study of dietary fat and risk of prostate cancer. *J Natl Cancer Inst*. 1993; 85: 1571-1579.
7. Whittemore AS, Kolonel LN, Wu AH, John EM, Gallagher RP, Howe GR, et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. *J Natl Cancer Inst*. 1995; 87: 652-661.
8. [No authors listed]. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin*. 2012; 62: 275-276.
9. Chan JM, Giovannucci EL. Vegetables, fruits, associated micronutrients, and risk of prostate cancer. *Epidemiol Rev*. 2001; 23: 82-86.
10. Spentzos D, Mantzoros C, Regan MM, Morrissey ME, Duggan S, Flickner-Garvey S, et al. Minimal effect of a low-fat/high soy diet for asymptomatic, hormonally naive prostate cancer patients. *Clin Cancer Res*. 2003; 9: 3282-3287.
11. Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA*. 2007; 297: 969-977.
12. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med*. 2008; 359: 229-241.
13. Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med*. 2004; 140: 769-777.
14. Ebbeling CB, Leidig MM, Feldman HA, Lovesky MM, Ludwig DS. Effects of a low-glycemic load vs low-fat diet in obese young adults: a randomized trial. *JAMA*. 2007; 297: 2092-2102.
15. Mukherjee P, Sotnikov AV, Mangian HJ, Zhou JR, Visek WJ, Clinton SK. Energy intake and prostate tumor growth, angiogenesis, and vascular endothelial growth factor expression. *J Natl Cancer Inst*. 1999; 91: 512-523.
16. Mavropoulos JC, Isaacs WB, Pizzo SV, Freedland SJ. Is there a role for a low-carbohydrate ketogenic diet in the management of prostate cancer? *Urology*. 2006; 68: 15-8.
17. Freedland SJ, Mavropoulos J, Wang A, Darshan M, Demark-Wahnefried W, Aronson WJ, et al. Carbohydrate restriction, prostate cancer growth, and the insulin-like growth factor axis. *Prostate*. 2008; 68: 11-19.
18. Venkateswaran V, Haddad AQ, Fleshner NE, Fan R, Sugar LM, Nam R, et al. Association of diet-induced hyperinsulinemia with accelerated growth of prostate cancer (LNCaP) xenografts. *J Natl Cancer Inst*. 2007; 99: 1793-1800.
19. Kasim-Karakas SE, Tsodikov A, Singh U, Jialal I. Responses of inflammatory markers to a low-fat, high-carbohydrate diet: effects of energy intake. *Am J Clin Nutr*. 2006; 83: 774-779.
20. McDonald AC, Vira MA, Vidal AC, Gan W, Freedland SJ et al. Association between systemic inflammatory markers and serum prostate-specific antigen in men without prostatic disease - the 2001-2008 National Health and Nutrition Examination Survey. *Prostate*. 2014; 74: 561-567.
21. Tymchuk CN, Barnard RJ, Heber D, Aronson WJ. Evidence of an inhibitory effect of diet and exercise on prostate cancer cell growth. *J Urol*. 2001; 166: 1185-1189.
22. Nebeling LC, Miraldi F, Shurin SB, Lerner E. Effects of a ketogenic diet on tumor metabolism and nutritional status in pediatric oncology patients: two case reports. *J Am Coll Nutr*. 1995; 14: 202-208.
23. Ornish D, Magbanua MJ, Weidner G, Weinberg V, Kemp C, Green C, et al. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. *Proc Natl Acad Sci U S A*. 2008; 105: 8369-8374.

Cite this article

Mavropoulos JC, Hite AH, Howard LE, Vidal AC, Banez LL, et al. (2015) Comparison of Low-Carbohydrate Vs. A Low-Fat Diet on Prostate Cancer Biomarkers. *J Transl Med Epidemiol* 3(1): 1036.