J Tokyo Wom Med Univ
77(3) 121～125 (2007)

Dietary Preferences of Patients with Prostate Cancer: Investigation at a Health-Screening Center

Shiro ONITSUKA, Atsushi MAEDA and **Nobuyuki GOYA***

Institute of Geriatrics, Tokyo Women's Medical University
*Department of Urology, Tokyo Women's Medical University, School of Medicine

(Accepted January 23, 2007)

One of the reasons for the differing incidence of prostate cancer between Asian and Western countries is diet, which is a socioenvironmental factor. In order to ascertain the effects of food and nutrient intake on prostate cancer, the present study investigated 2,500 men who underwent health screening at our Institute. Subjects were patients who were diagnosed with prostate cancer (n=39) and those without prostate cancer (patients in whom Prostate specific antigen (PSA) was consistently below 4.0 ng/ml over a two-year period, n=416). Questionnaires were used to ascertain food intake for three days before each health screening, and diet analysis software was used to compare food intake. For the prostate cancer patients, meat intake was significantly higher, and in terms of nutrients, vitamin A intake was higher, while vitamin D intake was lower. Vitamin A is abundant in animal meat and vitamin D is plentiful in seafood, thus suggesting a correlation between seafood intake and cancer cell suppression for the men without prostate cancer. The results suggest that it may be possible to lower the incidence of prostate cancer by recommending people to eat less meat and consume more seafood rich in vitamin D.

Key words: prostate cancer, Prostate specific antigen (PSA), food, meat, vitamin D

Introduction

The incidence of prostate cancer per 100,000 is 8 in Japan, 0.5 in China, 102 in the US, and 135 in Sweden[1], and one of the reasons for these differences in the incidence of prostate cancer between Western and Asian countries is diet, which is a socioenvironmental factor[2]. While cohort and case-control studies on the effects of diet have been conducted in Western countries, few such studies have been performed in Japan. Prostate cancer is characterized by high incidence and long disease duration, diagnostic utility of prostate specific antigen (PSA), and apparent involvement of certain hereditary and racial factors[3]. Hence, prostate cancer is a good target disease for cancer prevention. In Japan, prostate cancer is one of several malignancies that are increasing in frequency, and identifying foods and nutrients that are closely related to the onset and suppression of prostate cancer could aid prevention.

The Institute of Geriatrics, Tokyo Women's Medical University (IOG) provides membership-based health screening and periodic dietary guidance. The effects of diet on prostate cancer patients were investigated by comparing prostate cancer patients to men without prostate cancer; both groups had undergone screening at the above-mentioned facility.

Subjects and Methods

1. Subjects

At the IOG, 3,500 members undergo periodic health screenings, and of these, 2,500 are men. Of the 2,500 men, the following two groups were compared: men who were diagnosed with prostate cancer by prostate biopsy from April 1997 to March 2005 (cancer group), and those in whom PSA level was consistently below 4.0 mg/ml from 2002 to 2004 (a total of four screenings were performed; one every six months) (control group). We defined these continuous low PSA group as without prostate cancer group. PSA was measured using the Tandem-R

Table 1 Clinical characteristics

	Prostate cancer (n = 39)	Control (n = 416)
Age (yr)	70.1 ± 4.8 (range 60 ~ 79)	69.1 ± 5.1 (range 60 ~ 79)
Height (cm)	166.1 ± 4.5	165.7 ± 5.6
Weight (kg)	65.6 ± 6.9	65.2 ± 8.1
BMI	23.9 ± 2.4	23.7 ± 2.6

Table 2 Nutrient consumption

	Prostate cancer (n = 39)	Control (n = 416)
Kilocalories (kcal)	1,799 ± 294	1,852 ± 310
Carbohydrates (g)	259 ± 46	260 ± 51
Protein (g)	61.8 ± 13.0	65.3 ± 23.6
Fat (g)	42.5 ± 10.8	45.6 ± 23.9

Table 3 Food characteristics

Food (g)	Prostate cancer (n = 39)	Control (n = 416)
Grains	415.9 ± 105.6	421.0 ± 100.9
Tubers	53.3 ± 43.2	45.3 ± 38.2
Sugar	6.5 ± 1.9	7.1 ± 3.4
Beans	68.0 ± 47.8	65.7 ± 42.3
Vegetables	290.8 ± 168.9	252.2 ± 115.8
Fruits	132.6 ± 88.7	109.1 ± 73.6
Mushrooms	9.8 ± 6.6	8.5 ± 4.7
Seaweeds	3.8 ± 1.9	4.5 ± 6.6
Seafood *	57.2 ± 33.9	68.0 ± 38.2
Meat **	66.3 ± 88.8	51.4 ± 26.8
Eggs	23.8 ± 14.0	27.4 ± 18.2
Milk and dairy products	190.6 ± 128.8	195.9 ± 132.0

* $p = 0.09$, ** $p < 0.001$.

PSA Assay Kit (Yamasa Corporation, Chiba, Japan).

2. Methods

Based on questionnaires that were filled out for three days before each screening, food intake was analyzed using diet analysis software (WELLNESS®, Top Business System, Okayama, Japan). The amount and type of food intake were ascertained separately for main meals and snacks. For the cancer group, dietary intake prior to definitive diagnosis was analyzed, and for the control group, the most recent dietary intake was analyzed and the results were compared. A Student's t-test was used for analysis with the level of significance set at $p<0.05$.

Table 4 Nutritional characteristics

Nutrition	Prostate cancer (n = 39)	Control (n = 416)
Vitamins		
A (μgRE) *	1,826 ± 1,302	838 ± 623
B1 (mg)	0.84 ± 0.26	0.79 ± 0.20
B2 (mg)	1.13 ± 0.38	1.12 ± 0.60
C (mg)	115 ± 89	102 ± 89
D (μg) *	5.0 ± 2.2	7.0 ± 3.5
E (mgα-TE)	7.6 ± 1.2	6.8 ± 2.5
Calcium (mg)	534 ± 166	552 ± 239
Iron (mg)	6.6 ± 1.9	6.7 ± 1.7
Cholesterol (mg)	229 ± 73	256 ± 102
Fiber (g)	13.5 ± 4.4	12.4 ± 3.4

* $p < 0.001$.

Results

Of the 2,500 men, there were 39 prostate cancer patients (cancer group) and 416 men without prostate cancer who are defined as individuals with continuous low PSA levels (control group). Mean PSA velocity of control group was 0.05 ng/ml/year (range: −0.7-0.7). The average age for the prostate cancer group was 69.1 years, while that for the control group was 70.1 years; this was not a significant intergroup difference. There were also no significant intergroup differences in height, body weight or body mass index (Table 1). Moreover, the prostate cancer group and the control group did not differ significantly in terms of total energy intake (1,799 kcal vs. 1,852 kcal), and carbohydrate, protein, fat intake were also similar (Table 2).

In terms of dietary intake, meat intake for the prostate cancer group was 66.3 g, which was significantly greater than that for the control group at 51.4 g ($p<0.001$), and the amount of seafood intake for the prostate cancer group was 57.2 g, which was lower, albeit not significantly, than that for the control group at 68.0 g. There were no significant intergroup differences in consumption of eggs, milk products, grains, tubers, beans, or vegetables including mushrooms (Table 3).

In terms of nutrient intake, vitamin A intake for the prostate cancer group was 1,826 μ/gRE, which was significantly higher than that for the control group at 838 μ/gRE ($p<0.001$). Furthermore, vitamin D intake for the prostate cancer group was 5.0

μ/g, which was significantly lower than that for the control group at 7.0 μ/g ($p<0.001$). No significant intergroup differences were apparent in intake of vitamins B1, B2, C or E. Also, there were no significant intergroup differences in calcium and cholesterol (Table 4).

Discussion

The onset of prostate cancer involves socioenvironmental factors as well as racial factors. This is evident from the finding that the incidence of prostate cancer among Japanese American men in Hawaii is higher when compared to Japanese men in Japan, but lower when compared to American men in the US[4]. Of the socioenvironmental factors thought to be related to prostate cancer, diet has been receiving mounting interest. However, the preventative effects of diet on prostate cancer have not been clarified, and only one prospective study on nutrients and prostate cancer prevention found that vitamin E suppressed the onset of prostate cancer[5].

While several cohort and case-control studies have examined diet and nutrients in prostate cancer[6], few studies have quantified dietary contents, and it has not always been clear if control groups consisted of people without prostate cancer. In our study, diet analysis software (WELLNESS®) was used to quantity dietary intake, and as a control, men whose PSA level was ≤4.0 ng/ml over a two-year period were examined (PSA was measured every six months, a total of four times). In general, PSA is ≤4.0 ng/ml in several percent of prostate cancer patients[7], but we believe that the probability of prostate cancer is very low if PSA is consistently ≤4.0 ng/ml in four tests conducted over a two-year period and PSA velocity is under 0.75 ng/ml/year[8]. In fact, subsequent follow-up observations have shown that none of the control patients developed prostate cancer.

Vitamin A has animal- and plant-derived forms, and animal-derived vitamin A is found abundantly in chicken, liver, eggs, and milk products. In the present study, because meat intake was high for the prostate cancer group, there was a significant difference in vitamin A intake between the cancer and control groups. However, the plant- and animal-derived forms have different affects at the cellular level. β-carotene, in such foods as ginseng and broccoli, is converted into vitamin A in the gastrointestinal tract[9], and plant-derived vitamin A suppresses free radicals and nitrosamine, which are related to carcinogenesis. The preventative effects of plant-derived vitamin A on cancer have been documented by cohort and case-control studies[10][11].

Vitamin D is found in milk, seafood, and some plants such as mushrooms. One of the reasons for the significant difference in vitamin D intake between the cancer and control groups could have been the lower seafood intake in the cancer group. Experiment data have shown that prostate cancer cells have vitamin D receptors which suppress cellular growth, and vitamin D administration has been reported to suppress growth[12]. Moreover, one clinical study on recurrent cancer documented that active vitamin D administration lowered PSA. Unfortunately, there is no epidemiological data connecting prostate cancer onset and vitamin D intake.

However, vitamin D activation requires ultraviolet light, and mortality rate of prostate cancer per 100,000 is high in northern countries with less exposure to ultraviolet light: 20.8 in Norway, 18.9 in Sweden, 11.6 in Italy, and 7.9 in Greece[13]. This suggests a correlation between vitamin D and prostate cancer. Vitamin D is found abundantly in seafood and mushrooms that Japanese consume on a daily basis, and this could play a role in suppressing the onset of prostate cancer. In the present study, there was no significant intragroup difference in calcium intake, but calcium suppresses the synthesis of active vitamin D. Therefore, calcium interferes with the antitumor effects of vitamin D, and high calcium intake may be a risk factor for prostate cancer[14]. One cohort study found that milk and calcium intake was a risk factor for prostate cancer[15].

While dietary lipids are believed to be involved in the development of several cancers, including prostate cancer, breast cancer, and colon cancer, fat intake did not differ significantly between the cancer and control groups. The epidemiology of prostate cancer resembles that of breast cancer those have

high incident rate in recent Japanese[16], and the role of lipids in breast cancer carcinogenesis has been closely studied[17]. Lipid metabolites as well as lipids themselves are thought to be involved in carcinogenesis. Cholesterol is converted into androgen, which can facilitate the onset of prostate cancer[18].

The biggest difference between Asian and European diets is the intake of soybean products. Soybean lowers male hormones and possesses weak estrogenic effects. In the present study, there was no significant difference in soybean intake between the cancer and control groups[19].

In any case-control or cohort study investigating the relationship between diet and carcinogenesis, the main issue is whether or not surveyed dietary data reflect past dietary intake, which is important for cancer onset. In the present study, food intake was assessed over a three-day period, and as a result, we consider that data reflected subjects' dietary preferences.

In order to obtain evidence-based data for prevention of prostate cancer, more case-control and cohort studies will be needed.

Conclusions

Among the prostate cancer patients, meat intake was high, and vitamin D intake was low. The results suggest that it may be possible to lower the onset of prostate cancer by eating less meat and consuming more seafood and mushrooms rich in vitamin D.

The importance of preventative medicine is well recognized today, and we hope that there will be more epidemiological studies on prostate cancer, which is becoming increasingly prevalent in Japan.

Acknowledgement

We would like to thank Ms. Kotoji Fukunaga (dietician) at the Institute of Geriatrics, Tokyo Women's Medical University for her assistance.

References

1) **Nakata S, Ohtake N, Yamanaka H**: Epidemiological trends of prostate cancer in Japan and international comparisons. Nippon Rinsho **60**: 44–48, 2002
2) **Bostwick DG, Burke HB, Djakiew D et al**: Human prostate cancer risk factors. Cancer **101**: 2371–2490, 2004
3) **Marks LS, Kojima M, Demarzo A et al**: Prostate cancer in native Japanese and Japanese-American men: Effects of dietary differences on prostatic tissue. Urology **64**: 765–771, 2004
4) **Parkin DM, Pissani P, Ferlay J**: Global cancer statistics. CA Cancer J Clin **49**: 33–64, 1999
5) **Heinonen OP, Albanes D, Virtamo J et al**: Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. J Natl Cancer Inst **90**: 440–446, 1998
6) **Schulman CC, Ekane S, Zlotta AR**: Nutrition and prostate cancer: Evidence or suspicion? Urology **58**: 318–334, 2001
7) **Ito K, Kubota Y, Yamamoto T et al**: Long term follow-up of mass screening for prostate carcinoma in men with initial prostate specific antigen levels of 4.0 ng/ml or less. Cancer **91**: 744–751, 2001
8) **Carter HB, Pearson JD, Metter EJ et al**: Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. JAMA **267**: 2215–2220, 1992
9) **Machlin LJ, Bendich A**: Free radical tissue damage: protective role of antioxidant nutrients. FASEB J **1**: 441–445, 1987
10) **Anderson SO, Wolk A, Bergstrom R et al**: Energy, nutrient intake and prostate cancer: a population-based case-control study in Sweden. Int J Cancer **68**: 716–722, 1996
11) **Rohan TE, Howe GR, Burch JD et al**: Dietary factors and risk of prostate cancer: a case-control study in Ontario, Canada. Cancer Causes Control **6**: 145–154, 1999
12) **Chen TC, Schwartz GG, Burnstein KL et al**: The invitro evaluation of 25-hydroxyvitamin D3 and 19-nor-1 alpha, 25-dihydroxyvitamin D2 as therapeutic agents for prostate cancer. Clin Cancer Res **6**: 901–908, 2000
13) **Hanchette CL, Scwartz GG**: Geographic patterns of prostate cancer mortality: evidence for a protective effect of ultraviolet radiation. Cancer **70**: 2861–2869, 1992
14) **Grant WB**: Calcium, lycopen, vitamin D and prostate cancer. Prostate **42**: 243, 2000
15) **Grant WB**: An ecologic study of dietary links to prostate cancer. Altern Med Res **4**: 162–169, 1999
16) **The Research Group for Population-based Cancer Registration in Japan**: Cancer incidence and incidence rates in Japan in 1996: Estimates based on data from 10 population-based cancer registries. Jpn J Clin Oncol **31**: 410–414, 2001
17) **Demark-Wahnefried W, Peterson B, McBride C et al**: Current health behaviors and readiness to pursue life-style changes among men and women diagnosed with early stage prostate and breast carcinomas. Cancer **58**: 674–684, 2000
18) **Key TJ, Allen NE, Spencer EA et al**: The effect of diet on risk of cancer. Lancet **360**: 861–868, 2002
19) **Sonoda T, Nagata Y, Mori M et al**: A case-control study of diet and prostate cancer in Japan: possible protective effect of traditional Japanese diet. Cancer Sci **95**: 238–242, 2004

前立腺癌発生に及ぼす食事の影響—健診センターにおける検討—

東京女子医科大学附属成人医学センター
*東京女子医科大学医学部泌尿器科学
鬼塚（オニツカ）　史朗（シロウ）・前田（マエダ）　淳（アツシ）・合谷（ゴウヤ）　信行（ノブユキ）*

欧米とアジアの前立腺癌の発生率が異なる理由の一つとして，社会環境因子の一つである食事の差異があげられている．前立腺癌に対する食事，栄養素の影響を調べるため前立腺癌患者と非前立腺癌患者の摂取食事内容，摂取栄養素の違いについて検討した．東京女子医大成人医学センターにおける健康診断男性会員2,500名中，前立腺癌と診断された患者39名と，2年間6ヵ月毎に行った計4回の健康診断で，PSAが常に4.0 ng/ml以下の会員416名を対照（非前立腺癌患者）とし比較検討した．健康診断前3日間の食事質問票を用いて，前立腺癌患者は確定診断前の摂取内容を，対照は最新の摂取内容を食事分析ソフトで解析した．前立腺癌患者の食事では，肉類が有意に多く摂取されており，栄養素としてビタミンAの摂取が多く，ビタミンDの摂取が少なかった．肉類摂取と前立腺癌の発生の関連が疑われた．ビタミンAは動物性食品に多く含まれており，前立腺癌患者は肉類の摂取が多いため有意差がでた可能性が考えられた．ビタミンDは魚介類に多く含まれ，非前立腺癌患者での癌細胞の増殖抑制効果との関連が推察された．肉食を少なくし，ビタミンDが多く含まれる魚介類の摂取を勧めることにより，前立腺癌の発生を抑制する可能性が考えられた．