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·Original Article·

Mass screening-based case-control study of diet and prostate cancer in Changchun, China

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Abstract

Aim: To investigate possible correlation factors for prostate cancer by a population-based case-control study in China. **Methods:** We carried out a mass screening of prostate cancer in Changchun, China, using a prostate-specific antigen assisted by Japan International Cooperation Agency. From June 1998 to December 2000, 3 940 men over 50 years old were screened. Of these, 29 men were diagnosed with prostate cancer. We selected 28 cases and matched them with controls of low prostate-specific antigen value (< 4.1 ng/mL) by 1: 10 according to age and place of employment. A case-control study of diet and prostate cancer was then carried out. **Results:** After adjustment for education, body mass index (BMI), smoking, alcohol consumption, marriage and diet, intake of soybean product was discovered to be inversely related to prostate cancer. Men who consumed soybean product more than twice per week on different days had a multivariate odds ratio (OR) of 0.38 (95% confidence interval [CI], 0.13–1.12). In addition, men who consumed soybean products more than once per day had a multivariate OR of 0.29 (95% CI, 0.11–0.79) compared with men who consumed soybean products less than once per week. The *P* for trend was 0.02, which showed significant difference. There was no significant difference in *P* trend for any dairy food. Even when we matched the cases and controls by other criteria, we found that soybean food was the only preventive factor associated with prostate cancer. **Conclusion:** Our study suggests that consumption of soybeans, one of the most popular foods in Asia, would decrease the risk of prostate cancer. *(Asian J Androl 2008 Jul; 10: 551–560)*

Keywords: soybean; prostate cancer; case-control study; diet

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1 Introduction

There are many questions concerning prostate cancer. (1) Why do Asian men have a much lower incidence of prostate cancer compared to men from the US and Europe? Latent or clinically insignificant cancer of the prostate is found at autopsy at approximately the same rate in men from Asian countries as those from the USA

(approximately 30% of men aged over 50 years), but there are large differences in the clinical incidence rate and mortality. Is there a strong possibility that diet and nutrition play a prominent role in accelerating or inhibiting the process by which clinically significant prostate cancer develops? (2) Is the fact that the hormone-dependent cancers of the prostate and breast show the same incidence rate and lifetime risk (the correlation *r* is 0.81 in 21 countries [1] related to diet? (3) Chinese and Japanese men have the lowest incidence of prostate cancer in the world. Yet, why, when Japanese men from these countries migrate to the North America, does their risk of developing prostate cancer increase 10-fold compared to their counterparts in Japan and China? (4) Although it is relatively rare in China, an increase in the incidence of prostate cancer has been reported in recent years. What factors can account for this conspicuous increase?

Prostate-specific antigen (PSA) is a very important marker for prostate screening and prostate cancer detection [2, 3]. It is more suitable for screening than digital rectal examination (DRE) or transrectal ultrasound (TRUS). Cao *et al.* [4] reported that the sensitivity of PSA > 4.10 μg/L was 93.10%, and that the efficiency of DRE and TRUS was very low. Their results showed that the overall characteristics of the cases detected at that PSA cut-off differed very little from those detected with the regimen based on PSA, DRE and TRUS [5]. A DRE that is abnormal but not suspicious for cancer does not affect the overall performance characteristics of the cancer detection [6, 7]. For this reason, in China in 1996, we started mass screening based on serum PSA levels with the cooperation of Prof. Kuwahara of the Miyagi Prefecture Cancer Center in Japan. In 1999 our study received the support of Japan International Cooperation Agency [8–10]. At almost the same time, we began to conduct epidemiological studies in cooperation with Prof. Tsuji of Tohoku University, Japan.

It is very important to conduct epidemiological studies of diet and prostate cancer. There are few diet studies in China and, in particular, no population-based studies on prostate cancer. In order to reveal the dietetic factors that might be associated with prostate cancer, we investigated the consumption frequency of some foods commonly eaten in China and conducted a mass screening-based case-control study in Changchun, China.

2 Materials and methods

2.1 Mass screening of prostate cancer

We carried out a mass screening of prostate cancer, using serum PSA, in employees of selected companies and organizations based in the urban area of Changchun. DRE was not included in this screening because of its lack of sensitivity. The Principal of each company or organization we contacted invited men 50 years old and above, currently employed or retired, to participate in the screening. They came from six groups: community and army; factory; corporation; post and telecom office; government and academy; and university and technical school. From April 1998 to December 2000, a total of 4 808 men over 50 years old were invited and 3 940 men were screened with 81.94% participation rate. All the 3 940 men were interviewed and underwent a test to determine the concentration of their serum PSA. There were 872 men (22.13%) aged 50–59 years, 1 806 men (45.84%) aged 60–69 years, 1 164 men (29.54%) aged 70–79 years, and 98 men (2.49%) aged older than 80 years. The average age was 65.03 ± 7.55 years.

The participants were asked not to have a DRE during the 2 weeks before the study commenced. Trained interviewers and nurses went to every place of employment to take interviews and draw blood samples. The immunoenzymetric assay kit (CanAg Diagnostics, Gothenburg, Sweden) was used to determine the serum PSA concentration. If a man had a PSA concentration greater than 4.1 ng/mL, he would be informed by telephone. The TRUS-guided systematic sextant biopsy examinations were carried out by doctors who had been trained in Japan. Toshiba 340 Ultrasound-Guided Biopsy Systems (Toshiba, Tokyo, Japan) were used in this process. For prostate biopsy, a TRUS-guided systematic sextant six-core biopsy was conducted using a biopsy gun (Pro-Mag 1; MD Tech, Gainesville, USA) with an 18-G biopsy needle (2.2 biopsy needle; MD Tech). The prostate cancer cases were diagnosed by the biopsy sample.

We defined a PSA concentration of 4.1 ng/mL as a cut-off value to carry out a diagnostic work-up using a TRUS-guided systematic sextant biopsy examination. One hundred and ninety men (4.8%) were positive, and were recommended to have a biopsy. Of these, 116 men were referred for a biopsy, and 29 men were diagnosed with prostate cancer.

Clinical stages were used in accordance with the UICC

(Union Internationale Contre le Cancer) recommended tumor node metastasis system (1997) [11]. Of the 29 cases of prostate cancer, there were: 18 cases of stage B, with limited cancer within the prostate gland; seven cases in stage C, through prostatic capsule, Extracapsular and Seminal vesicles; and four cases in stage D, with distant metastasis. The pathological grades used were in accordance with the Gleason system and the World Health Organization system [12]. All cases were divided into three groups: three cases were well-differentiated (Gleason score 2–4); 12 were moderately-differentiated (Gleason score 5–7); and 14 were poorly-differentiated (Gleason score 8–10).

2.2 Selection of cases and controls

We intended to select all 29 cases as the study subjects, and 10 controls per case were planned, selected from screening participants whose PSA was less than 4.1 ng/mL after matching by age (± 2 years), and place of employment. The cases and controls were planned with a ratio of 1:10 according to age and place of employment. Thus, we selected 28 cases of prostate cancer from the 29 cases, and the other remaining case was excluded because, at the age of 89, there was only one man fulfilling the selecting standard of control. All of the 28 cases had a high serum value of more than 4.1 ng/mL and were diagnosed with adenocarcinoma by histopathology. The men were aged between 54 years and 82 years: one man was aged in his 50s; seven men in their 60s; 17 men in their 70s; three men in their 80s.

Controls were selected from men with a low PSA of less than 4.0 ng/mL from the same company. On the evidence of the questionnaire, they had shown no history of serious disease. In 28 cases, controls were selected by age (2 years younger or older than the study subject) and place of employment, matched by the rate 1:10.

2.3 Data collection

As the validity of interviewer questionnaires is more reliable than patient questionnaires, in this study, all the data collection for cases and controls was based entirely on interviewer questionnaires. All of the men were interviewed in their place of employment then had blood taken for a PSA test. All of the 28 cases and 280 controls were interviewed using questionnaires. The questionnaire content included demographics, diet, body size, smoking, alcohol consumption, marital status and medical history.

The dietary information was limited to the frequency of intake of 10 food items, selected to include the most frequently consumed foods of Chinese people. These included food groups commonly consumed in Changchun, consisting of the following items: tomatoes, carrots, green vegetables, soybean products, beef, pork, chicken, milk, fish and tea. The soybean products consisted of tofu and soy milk. The tea item included black tea, green tea and jasmine tea. The tomatoes and carrots categories referred to any type, raw or prepared. Green vegetables included green leafy vegetables cooked or raw, perhaps used in salad. The food frequency was divided into five categories: more than once per day; three to six times per week; once or twice per week; less than once per week and more than once per month; and never, or less than once per month.

The cigarette smoking data included smoking status, described as never former, or current. The former and current smokers were asked about the age they started and the number of cigarettes smoked per day. The former smokers were asked for the year they quit.

We asked the participants whether they still drank alcohol, had never drunk, or had recently stopped. Former and current drinkers were asked their age when they began drinking, and about each type of alcoholic beverage consumed (beer, wine, or hard liquor). We also asked about the quantity consumed of each alcoholic drink. We asked the former drinkers how many years had passed since they had quit.

Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Age at marrying and how long couples had lived apart were determined for all the participants. Prostate cancer family history was also assessed.

2.4 Statistical analyses

We calculated the age of screening (years), height (cm), weight (kg), BMI (kg/m^2), and the age at first marriage by the average mean. Education, cigarette smoking, and alcohol consumption were calculated using logistic regression methods with odds ratios (OR). The corresponding 95% confidence intervals (CI), crude and adjusted, for education (high school/other) and BMI (25+/other), were calculated.

Food intakes were categorized from five catalogs combined into three groups. Only green vegetables were combined to two groups. The OR and the corresponding 95% CI were calculated by multiple logistic regression. In the models, the following confounders were included:

education (high school/other), BMI (> 25 kg/m^2/other), smoking (never/former/current [1–19/day]/current [> 20/day]), alcohol consumption (current/no), and food frequency (tomatoes, green vegetables, soybean products, beef, pork and milk). Because neither cases nor controls had any family history of prostate cancer, we did not include family history in the models. Statistics were calculated using SPSS 10.0 (SPSS, Chicago, IL, USA).

3 Results

In this study, the men screened were from selected major companies and institutes located in the urban area of Changchun. They came from six groups: community and army; factory; corporation; post and telecom office; government and academy; and university and technical school. We analyzed the PSA-positive rate and cancer detection rate adjusted by age in each of the six groups. In all six groups there was a significant correlation of age-adjusted PSA-positive rate and age-adjusted cancer detection rate adjusted by secondary examination rate with Pearson's chi-square test ($r = 0.898$; $P < 0.01$) and Spearman's Rank Correlation test ($r = 1.000$; $P < 0.001$) [8]. Overall, age–adjusted PSA-positive rate was 4.80%, and the age-adjusted cancer detection rate was 0.78%. The university and technical school group had the highest PSA-positive rate of 5.72%, and the factory group had the lowest rate of 3.84%. After adjusting the secondary examination rate, the age-adjusted cancer detection rate reached 1.28%, the detection rate was the highest in the university and technical school group with 1.97%, and lowest in the factory group with 0.96%. Both the age-adjusted PSA-positive rate and age-adjusted cancer detection rate of the university and technical school group were significantly higher than the factory group (χ^2 test, $P < 0.05$).

Another important point is that men from the same company live in the same area because they have a company dormitory. All the participants from the six groups

Table 1. Distributions of characteristics of 28 prostate cancer patients and 280 controls participating in this study. –, not applicable; BMI, body mass index.

	Cases	Controls	*P* value
No. studied	28	280	–
Mean age (years)	71.39 ± 6.03	71.14 ± 5.78	0.82
Height (cm)	168.71 ± 6.08	168.78 ± 5.42	0.95
Weight (kg)	68.89 ± 9.98	67.38 ± 9.13	0.41
BMI	24.25 ± 3.61	23.66 ± 3.09	0.33

Table 2. Multivariate analysis of education, tobacco, alcohol and toxin contact history as related to prostate cancer risk in 28 prostate cancer patients and 280 controls. –, not applicable; CI, confidence interval; OR1, crude odds ratio; OR2, odds ratio adjusted for education (high school/other) and body mass index (BMI) (> 25 kg/m^2/other).

	Cases	Controls	OR1	95% CI	*P* for trend	OR2	95% CI	*P* for trend
Education (graduated from high school)								
No	10	127	1.00	–	–	1.00	–	–
Yes	18	153	1.64	0.65–4.15	0.30	1.74	0.67–4.51	0.26
Cigarette smoking								
Never	11	113	1.00	–	–	1.00	–	–
Former	5	70	0.74	0.25–2.20	–	0.75	0.25–2.25	–
Current (1–19/day)	5	49	1.05	0.35–3.16	–	1.19	0.39–3.68	–
Current (> 20/day)	7	48	1.53	0.55–4.29	0.44	1.80	0.62–5.22	0.45
Alcohol consumption								
Never	14	142	1.00	–	–	1.00	–	–
Previous	2	30	0.68	0.15–3.11	–	0.67	0.14–3.08	–
Current	12	108	1.13	0.50–2.56	0.81	1.11	0.49–2.54	0.81

live in six distinct areas in Changchun. For this reason, we matched the controls by age (2 years older or younger than the study subject) and place of employment. From Table 1, we can see the distributions of the characteris-

Table 3 Multivariate analysis of intake frequency of selected foods as related to prostate cancer risk in 28 prostate cancer patients and 280 controls. —, not applicable; CI, confidence interval; OR1, crude odds ratio; OR2, odds ratio adjusted for education (high school/other), body mass index (BMI) (> 25 kg/m^2/other), smoking (never/former/current [1–19/day]/current [> 20/day]), alcohol consumption (current/no), and food frequency (tomatoes, green vegetables, soybean products, beef, pork and milk).

Frequency	Cases	Controls	OR1	95% CI	*P* for trend	OR2	95% CI	*P* for trend
Tomatoes								
< 1/week	9	61	1.00	—	—	1.00	—	—
1–2/week	8	79	0.67	0.24–1.84	—	0.67	0.23–1.96	—
≥ 3/week	11	140	0.52	0.20–1.34	0.40	0.49	0.23–1.96	0.47
Carrots								
< 1/week	11	132	1.00	—	—	1.00	—	—
1–2/week	10	86	1.41	0.56–3.54	—	1.11	0.42–2.96	—
≥ 3/week	7	62	1.36	0.50–3.69	0.72	1.14	0.39–3.35	0.82
Green vegetables								
< 1/day	4	23	1.00	—	—	1.00	—	—
≥ 1/day	24	257	0.54	0.17–1.69	0.29	0.43	0.12–1.50	0.18
Soybean food (tofu and soy milk)								
≤ 2/week	11	51	1.00	—	—	1.00	—	—
3–6/week	7	88	0.47	0.17–1.27	—	0.38	0.13–1.12	—
≥ 1/day	10	141	0.36	0.14–0.92	0.04	0.29	0.11–0.79	0.02
Beef								
< 1/week	9	123	1.00	—	—	1.00	—	—
1–2/week	13	96	1.56	0.64–3.79	—	1.85	0.67–5.10	—
≥ 3/week	6	61	1.24	0.43–3.59	0.39	1.65	0.53–5.12	0.38
Pork								
≤ 2/week	4	78	1.00	—	—	1.00	—	—
3–6 /week	10	88	1.61	0.52–5.03	—	1.69	0.51–5.65	—
≥ 1/day	14	114	1.93	0.67–5.61	0.31	2.19	0.69–6.99	0.18
Chicken								
< 1/week	11	109	1.00	—	—	1.00	—	—
1–2/week	10	121	0.81	0.33–1.99	—	0.68	0.25–1.84	—
≥ 3/week	7	50	1.38	0.51–3.71	0.60	1.50	0.48–4.68	0.48
Fish								
< 1/week	11	111	1.00	—	—	1.00	—	—
1–2/week	12	119	1.02	0.42–2.46	—	1.14	0.43–3.00	—
≥ 3/week	5	50	1.01	0.32–3.18	0.99	0.88	0.25–3.03	0.88
Milk								
< 1/week	7	123	1.00	—	—	1.00	—	—
1–6 /week	9	79	1.98	0.72–5.46	—	1.60	0.50–5.16	—
≥ 1/day	12	78	2.68	1.02–7.06	0.14	2.41	0.72–8.03	0.15
Tea								
No	9	84	1.00	—	—	1.00	—	—
< 1/day	7	65	1.01	0.36–2.77	—	1.16	0.37–3.72	—
> 1/day	12	131	0.85	0.34–2.11	0.92	0.88	0.32–2.40	0.80

tics of prostate cancer patients and controls. There were no significant differences in age, height, or weight between cases and controls. There were also no significant differences in the average BMI values. The BMI of cases (24.25 ± 3.61) was more than that of controls (23.66 ± 3.09), although there was no significant difference in the statistics.

Table 2 shows the multivariate analysis of education, tobacco, and alcohol as related to prostate cancer. Compared with the group that did not graduate from high school, the group graduated from high school group had an OR of 1.74 (95% CI, 0.67–4.51) after adjustment for BMI (> 25 kg/m^2/other), although it did not affect the statistical difference. Cigarette smoking was divided into never, former, current (1–19/day), and current (> 20/day). Alcohol consumption was divided into never, former, and current. There were no significant differences in statistics for either drinking or smoking.

Table 3 shows comparisons of the data of selected foods associated with prostate cancer. We observed that red meat (beef and pork) and dairy milk had a *P* trend increased risk of prostate cancer, but there was no significant difference between the cases and controls. Consuming milk more than once per day had a crude OR of 2.68 (95% CI, 1.01–7.06), but after this was adjusted, the trend weakened. Neither the *P* for trend of crude or after adjustment affected the statistical difference. There were also no significant differences between cases and controls in the frequency of consumption of tomatoes, carrots, green vegetables, fish, chicken, or tea.

Interestingly, we found that higher consumption of soybean food products showed an inverse association with prostate cancer. The crude OR for men who consumed soybean more often than three times per week and less than once per day had a multivariate OR of 0.47 (95% CI, 0.17–1.27), and men consuming more than once per day had a multivariate OR of 0.36 (95% CI, 0.14–0.92) compared with men consuming less than one portion per week. The *P* trend was 0.039. After adjustment for education (high school/other), BMI (> 25 kg/m^2/other), smoking (never/former/current [1–19]/current [20]), alcohol consumption (current/no), marriage age (> 25 years/other), and food frequency (tomatoes, green vegetables, beef, pork, and milk), the trend was enhanced. The men who consumed tofu and soy milk more than three times per week and less than once a day had a multivariate OR of 0.38 (95% CI, 0.13–1.12). In addition, men consuming soybean products more than once a day had a multivariate OR of 0.29 (95% CI, 0.11–0.79) compared with men consuming less than once per week. The *P* trend was 0.02.

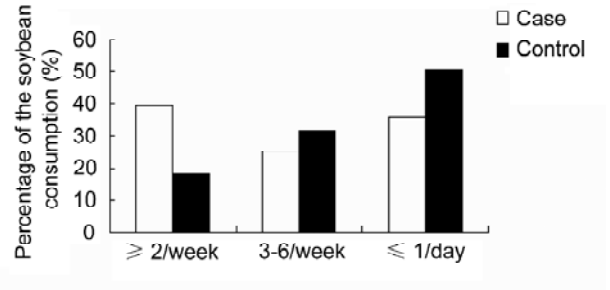

Figure 1. Comparison of soybean consumption in 28 prostate cancer patients and 280 controls.

We compared the three ratios of the consumption of soy food. As shown in Figure 1, the percentage of less than once per week, more often than three times per week and less than once a day, or more than once a day, were 18%, 31%, and 50% in controls, respectively, whereas they were 39%, 25%, and 36% in cases, respectively. The number of cases consuming less than once per week was approximately half compared with the control group.

To confirm our results, we analyzed the association between soybean foods and prostate cancer. We matched the cases and the controls by other criteria, including smoking, BMI, education, or alcohol consumption. We analyzed all 29 cases and 290 controls separately. As shown in Table 4, we also found that the intake of soybean products (tofu and soy milk) was inversely related to prostate cancer. The OR was approximately 0.3 by the 1:10 matching study. We did not find any significant association between other food items and prostate cancer.

Then we carried out a comparison by matching men who underwent a biopsy found to be negative for prostate cancer, but who had an elevated PSA level, with 87 control cases in a 1:3 matching fashion. We found that the OR reached 0.49. We observed the same *P* trend, a decreased risk of prostate cancer. The significant difference could not be shown because the controls numbered only 87, and we could only carry out a 1: 3 matching study. According to the research of our cooperation team in Natoli, in all the men who had an elevated PSA level but a negative bilpsy result, approximately 10%–20% would be detected and diagnosed to prostate cancer in the next three years by the following-up PSA test and secondary biopsy.

Table 4. Multivariate analysis of soybean foods as related to prostate cancer risk by matching different criteria in prostate cancer patients and controls. —, not applicable; CI, confidence interval; OR1, crude odds ratio; OR2, odds ratio adjusted for age.

Frequency of soybean food intake	Cases	Controls	OR1	95% CI	*P* for trend	OR2	95% CI	*P* for trend
Matched by level of education (1:10)								
≤ 2/week	11	50	1.00	—	—	1.00	—	—
3–6/week	8	96	0.38	0.15–1.01	—	0.43	0.15–1.19	—
≥ 1/day	10	144	0.32	0.13–0.79	0. 01	0.42	0.12–0.85	0. 03
Matched by body mass index (1:10)								
≤ 2/week	11	59	1.00	—	—	1.00	—	—
3–6/week	8	78	0.55	0.21–1.45	—	0.45	0.16–1.23	—
≥ 1/day	10	153	0.35	0.14–0.87	0.03	0.35	0.14–0.90	0.03
Matched by smoking status (1:10)								
≤ 2/week	11	51	1.00	—	—	1.00	—	—
3–6/week	8	86	0.43	0.17–1.27	—	0.42	0.17–1.32	—
≥ 1/day	10	153	0.31	0.12–0.76	0.02	0.28	0.11–0.75	0.01
Matched by alcohol consumption (1:10)								
≤ 2/week	11	52	1.00	—	—	1.00	—	—
3–6/week	8	89	0.43	0.16–1.13	—	0.43	0.15–1.20	—
≥ 1/day	10	149	0.32	0.13–0.79	0.02	0.28	0.11–0.75	0.02
Matched with men who underwent a biopsy negative for prostate cancer (1:3)								
≤ 2/week	11	10	1.00	—	—	1.00	—	—
3–6/week	8	24	0.61	0.20–1.80	—	0.59	0.20–1.18	—
≥ 1/day	10	43	0.42	0.15–1.16	0.37	0.49	0.17–1.37	0.35

4 Discussion

Descriptive data suggests that diet plays a major role in prostate cancer. Mortality from prostate cancer among Japanese men increases when they emigrate to North America, and dietary changes are thought to be a significant factor in the increase [13]. There are many studies of diet and prostate cancer in USA or Europe, but there are few epidemiological studies about Asian countries, especially China.

From June 1998 to December 2000, we conducted a mass screening of prostate cancer using serum PSA in 3 940 men over 50 years old in Changchun, China, and 29 men were diagnosed with prostate cancer. We carried out a case-control study and found that soybean foods had a protective effect against prostate cancer.

We should address the fact that the distribution of prostate cancer stages in China, with very high numbers of stages C and D prostate cancer, is unlike North America , and is even different from Japan in the Asian countries. In our other published paper [10], which compared the natural background of prostate cancer in Japan and China, mass checks with a PSA-based screening were carried out in Natori, Japan and Changchun, China using identical procedures. A total of 2 212 Japanese men and 3 566 Chinese men aged older than 55 years (from the group here 3 940 men were aged 50 years or above) were mass checked by PSA-based screening. The cancer detection rate was 0.8% and 2.1% in Changchun and Natori, respectively. With regard to pathological grading, the poorly- and moderately-differentiated cancers were in the majority in Changchun (26/28, 89%), higher than Natori (32/46, 70%). Because there was no diet investigation in Natori, Japan, we can not compare the diet differences between the two countries. But in our current study we found that intake of soybean products might be an important factor in decreasing the incidence of prostate cancer.

Changchun is a cultural city with many colleges and academies. But it has only 180 years of history, and most of its population consists of people who graduated or transferred to work during the years when the mod-

ern state of China was founded. In our studies, the cases and controls were selected from mass screening. The controls were selected by age and place of employment, matched by 1: 10. So the selection bias could be decreased, but can not be avoided completely. The controls in our study had a previous smoking rate of 59.69%, and a rate of education above high school level of 54.64%, which was close to another case-control study of prostate cancer in 12 Chinese cities (1989–1992) [14] that showed rates of 62.1% and 50.3%, respectively. We also provided an interview at the same time as the PSA test, so the recall bias could be avoided.

Race and age were regarded as the risk factors for prostate cancer. All of the subjects we studied were Chinese men over 50 years old. Age was used as a matching factor for cases and controls. Family history and sexual behavior were also considered as risk factors [15–18]. We put the age of first marriage into the multivariate models. Because neither cases nor controls had any family history of prostate cancer, we did not put family history into the models. BMI and social class perhaps influence prostate cancer, so we also put the level of education (high school/other) and BMI (> 25 kg/m^2/other) into the multivariate model [19–21].

Many epidemiological studies have reported on the relationship of dietary fat, meat, and milk to prostate cancer. Red meat is acknowledged and believed to be a contributing factor to developing prostate cancer. Eight case-control studies and three cohort studies reported the increased risk of prostate cancer associated with red meat intake [15, 22–27]. Some papers reported that intake of milk has been associated with prostate cancer. Six case-control studies and four cohort studies reported the increased risk of prostate cancer associated with milk intake [20, 26, 28–35]. According to some papers, consumption of tomato-based food and vegetables might reduce the risk of prostate cancer. Five case-control studies and three cohort studies reported the decreased risk of prostate cancer associated with high lycopene or tomatoes [31, 34, 36–41]. In our study, we observed that red meat (beef and pork) or milk could perhaps increase the risk of prostate cancer, but there were no significant differences in trends of the cases and controls. Consuming milk more than once per day had a crude OR of 2.677 (95% CI, 1.016–7.055), but after adjustment, the trend weakened. And neither the *P* for trend of crude or after adjustment reached the statistical difference. There was also no significant difference in cases and controls in the frequency of consumption of tomatoes, carrots, green vegetables, fish, chicken, or tea. Soybean food is the most conspicuous food difference between Asian and USA or Europe .

Four case-control studies [18, 31, 42, 43] and two cohort studies [40, 44] reported the protective effect of soy food, and the OR or RR (relative risk) ranged from 0.3 to 0.69. But two other case-control studies [45, 46] and one cohort study [47] did not reach the statistical differences. In our studies we found higher consumption of soybean food product, tofu and soy milk, had a protective effect against prostate cancer. Higher consumption of soybean food products had an inverse association with prostate cancer. Men who consumed soybean products more often than twice per week and less than once per day had a crude OR of 0.466 (95% CI, 0.17–1.27), and men consuming more than once per day had a crude OR of 0.356 (95% CI, 0.14–0.92) compared with men consuming less than once per week. The *P* trend was 0.039. After adjusting for education (high school/other), BMI (> 25 kg/m^2/other), smoking (never/former/current [1–19/day]/current [> 20/day]), alcohol consumption (current/no), and food frequency (tomatoes, green vegetables, beef, pork and milk), the men who consumed tofu and soy milk more than twice per week or less than once per day had a multivariate OR of 0.38 (95% CI, 0.13–1.12). In addition, men consuming soybean more than once per day had a multivariate OR of 0.29 (95% CI, 0.11–0.79) compared with the men consuming less than once per week. Even when we matched by other criterias, including smoking, BMI, education and alcohol consumption, we found almost the same results.

Soybean, a dietary staple in many parts of Asia, is a major source of the isoflavonoids daidzein and genistein [48]. The geometric mean levels of the plasma total individual isoflavinoid were 7–110 times higher in Japanese men than in Finnish men. Genistein, a tyrosine kinase inhibitor, occurred in the highest concentration. We can hypothesize that these high phytoestrogen levels could inhibit the growth of prostate cancer in Japanese men, and might explain the low mortality from prostate cancer in Japan [49]. Moreover, soy-derived isoflavone genistein is an inhibitor of several steroid-metabolizing enzymes. Phytoestrogens of soy foods perhaps act as anti-estrogens for binding to the estrogen receptor. This might explain why populations that consume significant amounts of soy (e.g., South-East Asia) have a reduced risk of estrogen-dependent cancer.

Our study emphasized the importance of soybean foods such as tofu and soy milk. The less regular use of soybean food in USA or Europe is perhaps an important risk factor in the incidence of prostate cancer.

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