

# Vasectomy and Prostate Cancer Risk in China<sup>1</sup>

Ann W. Hsing,<sup>2</sup> Run-Tian Wang, Fung-Liu Gu, Marion Lee, Tao Wang, Tai Jun Leng, Margaret Spitz, and William J. Blot

Epidemiology and Biostatistics Program, National Cancer Institute, Bethesda, Maryland 20892 [A. W. H., W. J. B.]; Department of Epidemiology and Biostatistics, University of California at San Francisco, San Francisco, California 94143 [M. L.]; Departments of Epidemiology [R. T. W., T. W.] and Urology [F. L. G.], Beijing Medical University, Beijing 10083, China; The Third Army Medical University, Beijing, China [T. J. L.]; and Department of Epidemiology, M. D. Anderson Cancer Center, University of Texas, Houston, Texas 77030 [M. S.]

## Abstract

**Vasectomy has been reported to be associated with an increased risk of prostate cancer in western countries. A hospital-based case-control study was conducted in 12 cities in China to evaluate the relationship between vasectomy and prostate cancer risk in China, a low-risk country with rising incidence and increasing use of vasectomy. Interviews were conducted with 138 histologically confirmed prostate cancer cases diagnosed during 1989–1992 and 638 controls (158 hospital cancer, 158 hospital noncancer, and 322 neighborhood controls) of similar ages. Vasectomy at least 10 years prior to interview was reported by 10% of the cases versus 3% of the controls. Odds ratios for prostate cancer associated with vasectomy were 2.0 (95% confidence interval, 0.7–6.1), 3.3 (95% confidence interval, 1.0–11.3), and 6.7 (95% confidence interval, 2.1–21.6), respectively, when hospital cancer, hospital noncancer, and neighborhood controls were used for comparison. Although detection bias is of concern, the data suggest that in China, men with a history of vasectomy may experience an increased risk of prostate cancer.**

## Introduction

Prostate cancer is the most common cancer in the United States and many western countries (1). China has the lowest incidence rates of prostate cancer among over 100 registries reporting to the Cancer Incidence in Five Continents study (1). Age-adjusted rates in Shanghai, for example, are 1.7/100,000, in contrast to 61.8 and 82.0 among white and black Americans, respectively (1). Rates among Chinese men have begun to rise at a relatively slow rate (1.4%/year) (2, 3).

Despite the substantial international variations and high rates of prostate cancer in the western world, the

etiology of prostate cancer is unknown (4). Recently, there has been increasing concern about prostate cancer risk among men with vasectomies, a widely accepted, simple, inexpensive, and effective method for male contraception (5). Results from three recent studies in the United States (two prospective studies and one large population-based case-control study) showed that having a vasectomy was associated with an increased risk of prostate cancer (6–8). Findings from past epidemiological studies have been inconsistent. Of 5 case-control studies, 1 found no excess risk (9), 1 reported nonsignificant excess risks (10), and 3 found significant excess risks (11–13), whereas 1 retrospective cohort study reported no excess risk (14, 15). The overall risk of prostate cancer among vasectomized men in these 6 studies combined was 1.5 ( $P < 0.05$ ), according to a recent meta-analysis (16). In most studies, the excess risk was more pronounced among men who had received their vasectomy before age 35 or more than 20 years previously. A recent report from an NIH Consensus Development Conference on vasectomy and prostate cancer, however, concluded that there is no firm evidence to support an etiological relationship between vasectomy and prostate cancer (17).

In China, about 2 million vasectomies have been performed every year since 1982 (18). It might be easier to detect an effect of vasectomy in China because prostate cancer risk remains low and thus other risk factors are less prevalent and less likely to confound or mask an association. As part of a hospital-based case-control study in 12 cities in China to determine etiological factors, we investigated the relationship between vasectomy and prostate cancer risk.

## Materials and Methods

Since prostate cancer is relatively rare in China, major teaching hospitals in 12 cities (Beijing, Shanghai, Tianjing, Chongqing, Chengdu, Guangzhou, Shuzhou, Xian, Wuhan, Shenyang, Wulumugi, and Lanzhou) participated in the study. Cases were patients between the ages of 50 and 89, residents of these 12 cities for more than 10 years, diagnosed during 1989–1992 with histologically-confirmed prostate cancer, and still alive at the time of the study. A total of 138 eligible cases were included in the study. For each index case, three types of controls were selected: one cancer control (with a cancer diagnosis other than cancers of the prostate, breast, colon, or genitourinary tract) and one noncancer control (excluding patients with coronary heart disease or an endocrine disease) from the same hospital, and two neighborhood controls. In China, by law, every household has to register with the Bureau of Public Security. From the household register, a roster of houses and eligible subjects (male and within 5 years of age) from the same neighborhood as the index case was compiled for the selection of neighborhood controls.

For all study subjects, information on demographic characteristics, occupation, physical activity, diet, medical

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<sup>2</sup> To whom requests for reprints should be addressed, at National Cancer Institute, Epidemiology and Biostatistics Program, EPN 415, 6130 Executive Boulevard, Bethesda, MD 20892.

Table 1 Selected characteristics of prostate cancer cases and controls, China, 1989–1992

Selected characteristics	Cases	Hospital cancer controls	Hospital noncancer controls	Neighborhood controls
	No. % <sup>a</sup>	No. %	No. %	No. %
Total	136 (100%)	158 (100%)	158 (100%)	322 (100%)
Age				
40–59	13 (9.6)	19 (12.0)	16 (10.1)	34 (10.6)
60–69	54 (39.7)	60 (38.0)	62 (39.2)	130 (40.4)
≥70	69 (50.7)	79 (50.0)	80 (50.6)	158 (49.1)
Marital status				
Never married	0 (0)	0 (0)	1 (0.6)	2 (0.6)
Married	108 (79.4)	143 (90.5)	139 (88.0)	269 (83.5)
Divorced/widowed	12 (8.8)	10 (6.3)	11 (7.0)	31 (9.6)
Remarried	16 (11.8)	5 (3.2)	7 (4.4)	20 (6.2)
Education				
Illiterate	18 (13.3)	16 (10.4)	11 (7.5)	33 (10.5)
Primary school	44 (32.6)	62 (40.3)	55 (37.4)	124 (39.6)
High school	41 (30.4)	49 (31.8)	50 (34.0)	86 (27.5)
College	32 (23.7)	27 (17.5)	31 (21.1)	70 (22.4)
Socioeconomic index				
Low	69 (50.7)	85 (53.8)	94 (60.3)	150 (46.6)
Medium	61 (44.9)	72 (45.6)	60 (38.5)	165 (51.2)
High	6 (4.4)	1 (0.6)	2 (1.3)	7 (2.2)
Alcohol use				
Never	44 (32.6)	38 (24.4)	43 (27.4)	135 (43.0) <sup>b</sup>
Ever	91 (67.4)	118 (75.6)	114 (72.6)	179 (57.0)
Benign prostatic hyperplasia				
No	62 (51.7)	133 (87.5) <sup>b</sup>	122 (82.4) <sup>b</sup>	261 (86.4) <sup>b</sup>
Yes	58 (48.3)	19 (12.5)	26 (17.6)	28 (13.6)
Prostatitis				
Never	87 (75.7)	141 (92.8) <sup>b</sup>	146 (95.4) <sup>b</sup>	278 (93.9) <sup>b</sup>
Ever	28 (24.3)	11 (7.2)	7 (4.6)	18 (6.1)
Body mass index (kg/m <sup>2</sup> )	22.8 (3.5) <sup>c</sup>	21.1 (3.4)	22.3 (3.6)	22.8 (3.4)

<sup>a</sup> Missing data not included.

<sup>b</sup>  $p < 0.05$ .

<sup>c</sup> Mean (SD).

history, and ever having had a vasectomy was elicited by a structured questionnaire in an in-person interview. Cases and hospital controls were interviewed at the hospital, whereas neighborhood controls were interviewed at home. Overall response rates were 79% for cases, 95% for hospital cancer, 98% for hospital noncancer, and 80% for neighborhood controls.

Odds ratios for prostate cancer were calculated by logistic regression analysis (19), adjusting for age (by 5-year group) and, when indicated, for other factors.

## Results

A total of 138 cases and 638 controls (158 cancer, 158 noncancer, and 322 neighborhood controls) were included in the analysis. Of the 138 cases, 9, 17, 25, and 33% were diagnosed at clinical stages A, B, C, and D, respectively, while 16% did not have clinical staging information. The median age of diagnosis was 69.

Selected characteristics of cases and controls are shown in Table 1. The cases and controls were similar with respect to age and body mass index, but cases were more likely to have remarried, to have a slightly higher education and socioeconomic index, and to have a history of benign prostatic hyperplasia or prostatitis.

A total of 16 cases (11.6%) and 17 controls (2.6%) reported a history of vasectomy. Of these, two cases had vasectomies within 1 year of prostate cancer diagnosis and

therefore were excluded from the analysis. The remaining 31 subjects had their vasectomies at least 10 years prior to the study. Regardless of the type of controls used for comparison, vasectomy was associated with an increased risk of prostate cancer (Table 2). Odds ratios were 2.0 (95% CI,<sup>3</sup> 0.7–6.1), 3.3 (95% CI, 1.0–11.3), and 6.7 (95% CI, 2.1–21.6), respectively, for comparisons with hospital cancer, hospital noncancer, and neighborhood controls. All the risks reported here were adjusted for marital status, socioeconomic index, alcohol use, and a history of benign prostatic hyperplasia or prostatitis. The significant excess risks persisted when the analysis was limited to cases with advanced stages (of 80 cases with stage C and D, 8 had had a vasectomy; odds ratio, 6.9; 95% CI, 1.8–25.8 using neighborhood controls). Numbers were too small to evaluate the effects of age at vasectomy and number of years since vasectomy.

## Discussion

Consistent with studies conducted in the United States (6–8, 10–13), we found that in a low-risk Chinese population, men with a vasectomy had a significantly increased risk of prostate cancer. On the basis of the most conserva-

<sup>3</sup> The abbreviation used is: CI, confidence interval.

Table 2 Adjusted odds ratios (OR)<sup>a</sup> for prostate cancer associated with vasectomy, by three types of controls in China

	Cases No.	Hospital cancer controls			Hospital noncancer controls			Neighborhood controls		
		No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI
Total	136 <sup>b</sup>	156			158			322		
Vasectomy										
No	122	149	1.0		154	1.0		316	1.0	
Yes	14	7	2.0	(0.7–6.1)	4	3.3	(1.0–11.3)	6	6.7	(2.1–21.6)

<sup>a</sup> Adjusted for marital status, socioeconomic index, alcohol use, benign prostatic hyperplasia, and prostatitis.

<sup>b</sup> Two cases who had vasectomy within 1 year of prostate cancer diagnosis were excluded.

tive estimate from the three control groups, risk of this cancer was more than twice as high among men with *versus* without vasectomies.

Similar to previous studies, selection, misclassification, and detection bias could have occurred in this study, and thus caution should be exercised when interpreting its results. Because vasectomy was not included in the routine family planning program in China until 1979, men who elected to have a vasectomy form a self-selected group that may be quite different from the general public. In a survey of 8800 farmers in Sichuan Province in China, vasectomized men were generally healthier than the nonvasectomized men, as measured by a lower prevalence of hypertension, heart disease, rheumatism, and asthma, although no differences in height, weight, body mass index, blood pressure, or serum cholesterol levels were found (20).

Misclassification of vasectomy is possible but should be minimal, since in China a vasectomy is performed almost exclusively for male contraception purposes (18). Information on vasectomy was derived purely from self-reporting. No validation of vasectomy was carried out, since 60% of the subjects who reported having a vasectomy had had the surgery prior to 1970 and many old medical records were destroyed during the cultural revolution. The procedure is one likely to be easily remembered, however, and underreporting by controls or overreporting by cases is thought to be unlikely. Nevertheless, we were surprised that vasectomy was reported twice as frequently in cancer as in neighborhood controls, although this difference was not statistically significant. National estimates of the age-specific prevalence of vasectomies for men over age 60 are not available, since vasectomy did not become a common method of male contraception in China until 1980. In this study, the prevalence of vasectomies among the different controls (2–4%) was slightly lower than that in United States white men (3–8%) of the same age group (8).

Only cases of prostate cancer (diagnosed between 1988 and 1992) who were still alive at the time of interview were included in the study. If the prevalence of vasectomy in deceased patients was lower than that reported by the surviving cases in the study (we have no reason to believe it was), we may have overestimated prostate cancer risk.

Detection bias is of greater concern. If men who had had a vasectomy were under closer medical surveillance or urological screening than men without a vasectomy, they would be more likely to have prostate cancer detected (usually at an earlier stage). Such a detection bias, however, should be minimal in China, since prostate cancer is rare, routine urological screening by digital rectal examination and/or transrectal ultrasound is uncommon, and screening with prostate-specific antigen did not become available in China until 1991. In addition, only 9% of the cases were

stage A and 58% were clinically advanced cases (stage C and D), suggesting that early detection and detection bias are minimal. Limiting analysis to advanced cases (stage C and D) did not materially change the results.

In summary, despite its limitations, this investigation, the first to assess the relationship between having had a vasectomy and prostate cancer risk among Chinese men, adds to the accumulating evidence that vasectomy may increase the risk of prostate cancer. Although it is premature to state that the relationship is causal, several plausible mechanisms have been proposed: a change in endocrine status; an alteration in systemic or local immunity; a variation in exposure of the prostate to cancer-enhancing growth factor and/or inhibitors of these factors; and a decrease in some unknown factors that may inhibit malignant growth (21). Findings from this study warrant further investigation into the vasectomy-prostate cancer hypothesis and the mechanisms by which vasectomy might influence prostate cancer risk.

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