Vasectomy and Risk of Prostate Cancer[1]

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Abstract

Most studies do not support an association between vasectomy and prostate cancer, but a few have suggested a link. Vasectomy is a common birth control method, and prostate cancer is the most frequently diagnosed solid tumor in men, making this a major public health question. This study was specifically designed to determine whether or not vasectomy is associated with risk of prostate cancer. To examine this issue, we conducted a population-based case-control study in King County, Washington. Interviews were completed with men ages 40–64 years newly diagnosed with prostate cancer between January 1993 and December 1996 who were ascertained through the Seattle-Puget Sound Surveillance, Epidemiology, and End Results (SEER) cancer registry ($n = 753$) and with comparison men without prostate cancer identified from the same general population ($n = 703$). The odds ratio (OR) for prostate cancer in relation to vasectomy was assessed. The prevalence of vasectomy was similar in cases (39.4%) and controls (37.7%), resulting in no association (adjusted OR, 1.10; 95% confidence interval, 0.9–1.4). There was no consistent evidence that risk varied by the age at which vasectomy was performed, the time since vasectomy, or the calendar period when the vasectomy was performed. The OR in relation to vasectomy was higher in men with less aggressive prostate cancer. Risk estimates did not differ according to age, race, or family history of prostate cancer. This study suggests that vasectomy is not associated with the risk of developing prostate cancer. It also provides evidence that vasectomized men may be more likely to present with earlier-stage, lower-grade prostate tumors.

Introduction

The possible association between vasectomy and risk of prostate cancer is a major public health concern. Vasectomy is a widespread and extremely effective method of contraception, with an estimated 500,000 American men undergoing the procedure each year (1, 2). Prostate cancer is the most common cancer among United States men, and in 1999 alone, over 179,000 men will be newly diagnosed with the disease (3). Thus, earlier studies suggesting a potential relationship between prostate cancer incidence and vasectomy have raised apprehension among both vasectomized men and health care providers.

Results from previous epidemiological studies of vasectomy and prostate cancer have been inconsistent. Four (4–7) case-control studies using hospital-based controls reported positive associations between vasectomy and risk of prostate cancer, although subsequent hospital-based (8, 9) and population-based case-control studies refuted such an association (10–14). Two cohort studies (15, 16) estimated about a 60% increase in the RR[3] of prostate cancer in relation to vasectomy. However, a third large cohort study failed to observe any association between prostate cancer incidence and vasectomy (17).

Most of the previous studies were based on secondary analyses of data collected for other purposes and were not designed to assess vasectomy in relation to the risk of prostate cancer. The majority of these earlier studies also did not collect data on DRE or serum PSA testing, which became available in 1986, to evaluate potential detection bias related to screening for prostate cancer. These screening procedures may be correlated with vasectomy status as well as the diagnosis of prostate cancer. We hypothesize that men who get a vasectomy may also be more likely to seek prostate cancer screening and early care for prostate cancer. Thus, failure to control carefully for screening history may result in spurious elevations in risk estimates associated with vasectomy. Here we report the results of a large population-based case-control study that was specifically designed to address the question of whether or not vasectomy is associated with the risk of developing prostate cancer.

Materials and Methods

Study Subjects. Caucasian and African-American male residents of King County in northwestern Washington State, 40–64 years of age, who were newly diagnosed with histologically confirmed prostate cancer between January 1, 1993 and December 31, 1996 were eligible. Cases were identified from the Seattle-Puget Sound cancer registry, which has been part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program since 1974. The goal was to oversample younger men, because vasectomy did not became a common form of contraception until the 1960s. Only more

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[3] The abbreviations used are: RR, relative risk; DRE, digital rectal examination; PSA, prostate-specific antigen; OR, odds ratio; CI, confidence interval; BPH, benign prostatic hyperplasia.

recent cohorts of men had sufficient opportunity for exposure. For this reason, we included as eligible 100% of cases with ages less than 60 years at diagnosis and a random 75% sample of those who were age 60–64 years at diagnosis. We restricted our ascertainment to cases who had a residential telephone at the time of the cancer diagnosis because random digit dialing was the method used to select controls. During the ascertainment period, we identified 1055 eligible prostate cancer patients and excluded 138 cases due to the sampling protocol. We interviewed 753 of the 917 (82.1%) eligible, selected men with incident prostate cancer. Reasons for nonresponse included physician refusal to allow patient contact (2.6%), patient refusal (12.5%), inability to locate the patient (1.5%), patient inability to participate due to illness (0.4%), and death (0.2%). A brief telephone nonrespondent questionnaire was completed by 35 (26.7%) of the patients who refused to participate in the more extensive, in-person interview.

Male 40–64-year-old residents of King County, Washington were identified as a comparison group through random digit telephone dialing using a clustering factor of five residences per sampling unit (18, 19). Controls were frequency-matched to cases by age (same 5-year group) and recruited evenly throughout the ascertainment period of cases. During the first step of random digit dialing, complete household census information was obtained for 94% of the 21,116 residential telephone numbers contacted. We identified a total of 941 men who met the study eligibility criteria and agreed to receive information about the study. Of these, 703 (74.7%) were interviewed, 228 (24.2%) refused, 6 were lost to follow-up, and 4 were too ill to participate. The overall level of participation for controls was 70.2% (94% × 74.7%). In addition, 66 (27.7%) of those who refused to participate in the detailed interview completed a brief telephone nonrespondent interview.

Data Collection. Before the interview, all subjects signed informed consent for participation, and all study forms and procedures were approved by the Fred Hutchinson Cancer Research Center Institutional Review Board. Study subjects completed in-person interviews conducted by trained male interviewers using a standardized questionnaire. The questions pertained to the time period up to the date of cancer diagnosis for cases and a similar, randomly preassigned reference date for controls, which approximated the distribution of cases' diagnosis dates. Information on the following topics was elicited: (*a*) social and demographic factors; (*b*) physical development, height, weight, and physical activity; (*c*) reproductive history; (*d*) detailed medical history including genitourinary diseases, symptoms and procedures, and screening for prostate cancer; (*e*) vasectomy status including ever, reason for vasectomy, age at procedure, and year of procedure; (*f*) family structure and cancer history; (*g*) smoking and lifetime alcohol consumption; (*h*) lifetime sexual history; and (*i*) occupational history. A separate section of the study questionnaire administered to cases only asked about physical signs and symptoms before diagnosis and at the time of prostate cancer diagnosis. A chronological list of potential signs, symptoms, and tests or procedures that led to the diagnosis of prostate cancer was recorded, which allowed stratification of cases by the presence or absence of symptoms at diagnosis. A calendar of life events including marriages and births was used to enhance recall and record details such as age and date of the vasectomy and screening tests for the detection of prostate cancer, *i.e.*, PSA blood tests, DREs, and prostate ultrasound examinations. After the interview, each subject was asked to provide consent for the access to medical records. All subjects were then asked to complete a self-administered food frequency questionnaire about usual dietary intake during the 3–5 years before the reference date.

Subjects who refused the in-person interview were offered the opportunity to complete a brief telephone nonrespondent questionnaire. Information was obtained on demographic factors, height, weight, screening for prostate cancer, vasectomy status and age at procedure, and family history of prostate cancer in first-degree relatives.

Clinical information on prostate cancer cases was available from the Seattle-Puget Sound SEER cancer registry. Tumor histological grade was coded according to the Gleason system as follows: Gleason grade of 2–4, low grade (well differentiated); Gleason grade of 5–7, moderate grade; and Gleason grade of 8–10, high grade (poorly differentiated; Ref. 20). The stage at diagnosis was based on the Whitmore-Jewett system (21) and incorporated the best available clinical and pathological information obtained within 4 months of diagnosis. For men not undergoing radical prostatectomy, stage was based solely on clinical information. Surgical and pathological data were incorporated into the staging for men who had radical prostatectomy. For this analysis, stage A represents incidentally found disease confined to the prostate, stage B represents localized disease confined to the prostate, stage C represents regional disease that has spread beyond the prostate, and stage D represents metastatic disease.

For study subjects who were members of Group Health Cooperative, a large health maintenance organization in Washington State, medical records were reviewed to verify self-reported information on vasectomy status. Hospital and clinical data were available for 83.3% (65 of 78) of cases and 72.8% (67 of 92) of controls providing consent for access to medical records. Of the 132 records reviewed, there were 8 cases and 11 controls whose vasectomy was done at Group Health Cooperative according to the in-person interview data. All 19 (100%) of the self-reported vasectomies in these men were confirmed by medical records.

Statistical Analysis. ORs were calculated as estimates of the RR of prostate cancer associated with various parameters of vasectomy such as ever having undergone the procedure, age at vasectomy, and date of vasectomy. Logistic regression models were used to compute ORs and estimate 95% CIs around the point estimates of risk (22). To evaluate whether risk related to vasectomy varied by clinical factors such as histological tumor grade, stage of disease at diagnosis, and the presence of symptoms at the time of prostate cancer diagnosis, case strata were compared to controls using polychotomous logistic regression (23). For these analyses, tumor stage and grade were modeled as categorical outcomes. Differences in the distribution of potentially confounding factors in control men with and without vasectomy were evaluated using a χ^2 test. Differences in means between cases and controls were assessed by the *t* test, and all *P*s were two-sided. Tests for linear trends in risk estimates were performed by constructing scored variables that were entered into logistic models as continuous covariates. Multiplicative effect modification was evaluated by comparing the significance of the difference between models including and excluding the interaction term.

Established and suspected prostate cancer risk factors were examined for potential confounding effects on the vasectomy-prostate cancer association, including the following: (*a*) age at reference date; (*b*) race; (*c*) family history of prostate cancer (none, first-degree relatives, second-degree relatives only); (*d*) marital status; (*e*) income; (*f*) education; (*g*) religious preference; (*h*) smoking history; (*i*) alcohol consumption; (*j*)

weight, height, and body mass index; (*k*) sexual history (age at first intercourse, number of partners, history of sexually transmitted diseases); (*l*) history of BPH diagnosed by a physician >2 years before reference date; (*m*) detailed measures of screening for prostatic disease (ever had, frequency and recency of DREs, PSA blood tests, prostate ultrasounds, other urological procedures, visits to urologists); and (*n*) dietary intake (total fat, total saturated fat, lycopene, and β-carotene, all adjusted for total energy). Each of these variables was added one at a time to a model containing age and vasectomy status to assess confounding, which was considered if the factor changed the OR by more than 5%. Final logistic regression models controlled for the confounding effects of age (continuous), race, family history of prostate cancer, and the number of PSA tests within the 5 years before the reference date (0, 1–2, 3–4, and ≥5). The potential variation in RR estimates was also examined according to strata of age, race, family history of prostate cancer, and history of BPH to assess whether any subgroups experienced alterations in the RR associated with vasectomy.

Results

The distributions of control men according to vasectomy status and potential risk factors for prostate cancer were examined to identify variables that might confound the vasectomy-prostate cancer relationship. As shown in Table 1, vasectomized controls were more likely to be <60 years, white, and married or living as married at the reference date and to have a slightly higher annual income, previously seen a urologist, report a clinical history of BPH, report being a regular consumer of alcoholic beverages (drinking more than once monthly for ≥6 months), report religious preference as Protestant or another religion other than Catholic or Jewish, and a slightly higher frequency of having DREs and PSA blood tests done within the 5-year period before the reference date.

The overall frequency of vasectomy was similar in prostate cancer cases (39.4%) and comparison men (37.7%), which resulted in no association with ever having had a vasectomy (adjusted OR, 1.10; 95% CI, 0.9–1.4). The mean age at which vasectomy was performed in prostate cancer patients was 35.9 years compared to 36.3 years among controls ($P = 0.59$), and RR estimates did not differ according to the age at which the procedure was done (Table 2). For example, men who had a vasectomy at age 20–29 years had an OR of 1.15, and those who had the procedure at age 40 or older had an OR of 0.96.

The time interval after vasectomy was examined as the potential latency period between exposure and disease. The mean number of years since vasectomy was slightly greater in cases (21.7 years) compared to controls (20.3 years), but there was no evidence that men who had the procedure from 15 to more than 30 years in the past experienced a significant alteration in risk (trend $P = 0.11$). We also evaluated risk according to the calendar period when the procedure was done (Table 2). Again, there was no clear evidence that the ORs varied by the years during which the procedure was performed (trend $P = 0.09$). The average year of vasectomy was 1973 for cases and 1974 for controls.

Stage of disease, tumor histological grade, and the presence of symptoms at the time of diagnosis were also evaluated. As shown in Table 3, ORs associating vasectomy with prostate cancer were higher in men with lower-stage disease, in men with tumors that were well differentiated to moderately well differentiated, and among men who were asymptomatic at the time of prostate cancer diagnosis, although none of these ORs achieved statistical significance.

The relation between vasectomy and prostate cancer was further examined according to recognized risk factors for the

Table 1 Distribution of potential confounding factors (%) among control men without and with vasectomy, King County, Washington, 1993–1996

Factor	Controls without vasectomy ($n = 438$)	Controls with vasectomy ($n = 265$)
Age at reference date (yrs)		
40–49	8.4	7.9
50–54	18.3	21.9
55–59	35.6	40.8
60–64	37.7	29.4
Race		
Caucasian	96.4	99.2
African-American	3.6	0.8
Family history of prostate cancer		
None	85.2	83.4
First-degree relative	8.4	12.1
Second-degree relative	6.4	4.5
Marital status		
Married	77.6	87.5
Single	5.7	0
Other	16.7	12.5
Annual income ($)		
<30,000	15.7	8.3
30,000–49,999	25.6	21.9
50,000–74,999	23.3	33.2
75,000–99,999	16.7	17.4
≥100,000	17.6	17.7
Unknown	1.1	1.5
Education		
High school or less	23.0	23.8
Some college	19.4	28.3
College graduate	28.8	24.9
Graduate/professional school	28.8	23.0
Ever visited a urologist	33.1	38.5
History of BPH[a]	10.3	15.1
Current smoker[b]	16.0	15.5
Regular consumer of alcoholic beverages[c]	86.1	90.6
Religious preference		
Protestant/other	60.3	65.7
Catholic	17.6	12.5
Jewish	2.3	0.8
None	19.9	21.1
Hospitalized within the past year		
No	85.6	86.8
Yes	14.4	13.2
No. of physical exams within past 5 years		
0	12.6	10.9
1–2	36.5	37.7
3–4	19.2	20.8
≥5	31.7	30.6
No. of DREs within past 5 years		
0	14.6	16.6
1–2	41.1	37.0
3–4	25.6	20.7
≥5	23.7	25.7
No. of PSAs within past 5 years		
0	66.4	67.9
1–2	20.8	16.2
3–4	7.8	9.4
≥5	5.0	6.4

[a] BPH diagnosed by a physician >2 years before reference date.
[b] Current smoker is defined as smoking at reference date.
[c] Regular consumer is defined as ≥ monthly drinking of alcoholic beverages for ≥6 months.

Table 2 ORs and 95% CIs for the association of vasectomy with risk of prostate cancer, King County, Washington, 1993–1996

Vasectomy status	No. (%) of cases	No. (%) of controls	OR[a]	95% CI
Ever				
No	456 (60.6)	438 (62.3)	1.00[b]	
Yes	297 (39.4)	265 (37.7)	1.10	0.9–1.4
Age at vasectomy				
20–29 yrs	49 (6.5)	47 (6.7)	1.15	0.7–1.8
30–34 yrs	84 (11.2)	66 (9.4)	1.30	0.9–1.9
35–39 yrs	82 (10.9)	74 (10.5)	1.07	0.7–1.6
≥40 yrs	82 (10.9)	77 (11.0)	0.96	0.7–1.4
			Trend test[d]	$P = 0.24$
Years since vasectomy[c]				
<5	8 (1.1)	10 (1.4)	0.68	0.2–1.9
5–9	14 (1.9)	21 (3.0)	0.68	0.3–1.5
10–14	30 (4.0)	35 (5.0)	0.94	0.5–1.6
15–19	63 (8.4)	58 (8.3)	1.11	0.7–1.7
20–24	81 (10.8)	64 (9.1)	1.11	0.8–1.6
25–29	63 (8.4)	46 (6.5)	1.42	0.9–2.2
≥30	38 (5.0)	30 (4.3)	1.23	0.7–2.1
			Trend test[d]	$P = 0.11$
Year of vasectomy				
1952–1968	81 (10.8)	61 (8.7)	1.37	0.9–2.0
1969–1974	100 (13.1)	80 (11.4)	1.16	0.8–1.7
1975–1979	62 (8.2)	61 (8.7)	1.01	0.7–1.5
1980–1984	34 (4.5)	31 (4.4)	1.14	0.7–1.9
1985–1989	8 (1.1)	21 (3.0)	0.38	0.1–0.9
1990–1995	12 (1.6)	10 (1.4)	1.00	0.4–2.6
			Trend test[d]	$P = 0.09$

[a] Adjusted for age (continuous), race, family history of prostate cancer (none, first-degree relative, second-degree relative only), and number of PSA blood tests within 5 years before the reference date (0, 1–2, 3–4, ≥5).
[b] Reference group for all ORs related to vasectomy.
[c] Analysis excludes one control with missing information.
[d] Trend test based on exposed subjects only.

disease. We looked for effect modification by age, race, family history of prostate cancer, and a history of BPH. There was no evidence that RR estimates differed substantially in any of these subgroups.

We also calculated ORs associated with ever having had a vasectomy (OR, 1.10) after excluding study subjects according to other factors that may be associated with detection bias, undiagnosed prostate cancer in the control group, or latency period between vasectomy and reference date. No substantial change in RR estimates was noted after the exclusion of cases ($n = 114$) with stage A prostate cancer (OR, 1.08), after the exclusion of controls ($n = 43$) who reported never having had a DRE exam (OR, 1.12), after the exclusion of controls ($n = 44$) whose most recent PSA test was done as a follow-up for a prior prostate problem (OR, 1.08), including an earlier elevated PSA level ($n = 6$), and after the exclusion of subjects ($n = 8$ cases, 10 controls) whose vasectomy was performed within 5 years of the reference date (OR, 1.12).

Lastly, we estimated RR based on including vasectomy data (ever/never) provided by nonrespondents (35 cases and 66 controls). The OR for prostate cancer associated with vasectomy was similar if the nonrespondent data were added to the analysis (OR, 1.11), or if the percentages of vasectomized and nonvasectomized subjects who completed a nonrespondent questionnaire were applied to all nonrespondents (115 cases and 228 controls) to estimate the expected number of vasectomized and nonvasectomized cases and controls if all eligible subjects had agreed to participate (OR, 1.08).

Discussion

In this large population-based case-control investigation, which was specifically designed to address the question of whether or not vasectomy altered the risk of prostate cancer, we did not find consistent evidence that a history of vasectomy, age at which vasectomy was performed, time interval since vasectomy, or the time period during which the surgery was done was associated with the development of prostate cancer. Furthermore, RR estimates related to vasectomy did not vary substantially across different subgroups of men defined by age, race, family history of prostate cancer, or a history of BPH.

However, several potential limitations of the study deserve comment. It is possible that vasectomy status may have differed in subjects who did not participate in the study relative to those who completed the in-person interview. Some information was available from the nonrespondent telephone interview completed by 30.4% (35 of 115) of cases and 27.7% (66 of 238) of eligible controls, although this sample may not be representative of all nonrespondents. Even so, incorporating this information into the analysis did not alter the risk estimates associated with vasectomy.

It is also possible that some control men may have had undiagnosed prostatic cancer, leading to misclassification of disease and attenuation of the risk estimates toward the null. However, over 94% of the controls in this study reported that they had previously had a DRE examination and/or PSA test for the detection of prostate cancer. An earlier case-control study of men ages <85 years that measured PSA levels in controls found that only 11% of men in this older age group had values > 4.4 ng/ml (13). There were no differences in the proportions of vasectomized *versus* nonvasectomized controls who had an elevated PSA level in either Caucasian or African-American men (13). In our analysis, we noted no change in risk estimates when controls who reported that they had never had a DRE examination or those whose most recent PSA test was performed as a follow-up examination for an earlier prostate problem or an elevated PSA were excluded. Given that all of the controls in our study were less than 65 years of age, we would expect that only about 5% might have an elevated PSA level, and fewer still would have undiagnosed prostate cancer, based on experience from prostate cancer screening programs. Thus, it seems unlikely that this situation could have substantially affected our risk estimates.

Another possible limitation is the use of self-reported exposure data. Few of the earlier studies attempted to validate vasectomy status by medical record review, although reporting bias may occur. We attempted to deal with this issue in several ways. First, we only used male interviewers. Some study subjects may have considered the questions on vasectomy sensitive; such men may have felt more comfortable providing accurate information to male interviewers. Second, we used a calendar to record major life events such as marriage and births to assist with recall regarding the date of vasectomy for those who had had the procedure performed. The questionnaire included queries about vasectomy status in two different sections, under birth control methods and medical history and procedures. Lastly, our medical record validation substudy confirmed 100% of the self-reported vasectomy procedures.

Some earlier studies observed higher RR estimates in men with less advanced prostate cancer (4, 8, 16), perhaps indicating a correlation between vasectomy status and access to medical care or other lifestyle factors such as screening for prostate cancer. However, these prior studies did not collect sufficient information on DRE and PSA screening tests to evaluate the

Table 3 ORs for the association of vasectomy with risk of prostate cancer according to clinical characteristics of cancer patients, King County, Washington, 1993–1996

Characteristic	Vasectomy status		OR[a]	95% CI
	No (n = 456)	Yes (n = 297)		
Stage at diagnosis				
A	66 (14.5)[b]	48 (16.2)	1.19	0.8–1.8
B	262 (57.5)	177 (59.6)	1.16	0.9–1.5
C	77 (16.9)	47 (15.8)	1.04	0.7–1.6
D	39 (8.6)	18 (6.1)	0.78	0.4–1.4
Unk	12 (2.6)	7 (2.4)		
Gleason grade				
2–4	51 (11.2)	35 (11.8)	1.23	0.8–2.0
5–7	318 (69.7)	228 (76.8)	1.22	0.9–1.6
8–10	80 (17.5)	31 (10.4)	0.66	0.4–1.0
Unk	7 (1.5)	3 (1.0)		
Symptoms[c] at diagnosis				
No	297 (65.1)	206 (69.4)	1.14	0.9–1.5
Yes	159 (34.9)	90 (30.3)	1.02	0.7–1.4

[a] ORs for each stratum of cases compared to the same set of controls (438 with vasectomy, 265 without vasectomy), computed by polychotomous logistic regression; ORs adjusted for age (continuous), race, family history of prostate cancer (none, first-degree relative, second-degree relative only), and number of PSA blood tests within 5 years before reference date (0, 1–2, 3–4, ≥5).
[b] Data represent the number of cases followed by the percentage of cases in parentheses.
[c] One case had missing information on symptoms at diagnosis; this variable was based on whether the patient reported having any symptoms at the time of the initial physician visit which led to the diagnosis of prostate cancer.

issue. In our data, the pattern of RRs suggests that vasectomized men may be more likely to present earlier in the course of their disease, which may in fact reflect a higher intensity of screening in this population. Our RR estimate associated with vasectomy was positively confounded by the frequency of PSA testing within the 5 years before the reference date.

Inconclusive results regarding vasectomy and prostate cancer have been reported from prior studies (24), and indisputable concerns about the roles of detection bias, selection bias, unmeasured confounding, and chance as explanations for what are relatively weak positive results have been raised (25, 26). Most of the previous investigations were not designed to address this possible association and were based on analyses of data collected for other purposes. Of 11 prior case-control studies, 7 found no association (8–14), and 4 found elevated risk estimates (4–7). All of these latter studies included hospitalized controls, who may have underrepresented the frequency of vasectomy in the populations from which cases were ascertained (27). Such a selection bias may have produced inflated risk estimates. One of the first positive case-control studies was from a hospital-based medical surveillance program that reported an initial RR estimate of 5.3 (95% CI ,2.7–10.0; Ref. 4). With subsequent data collection, this estimate fell to 1.2 (95% CI, 0.6–2.7; Ref. 8). Guess (25) has commented on the tendency of medical surveillance studies to produce upwardly biased RRs.

Several cohort studies have also been published. A large retrospective cohort study by Sidney *et al.* (17, 28) found no evidence that vasectomy was associated with prostate cancer. In another retrospective cohort study by Giovannucci *et al.* (15), vasectomy was linked to a 60% increase in risk. This study involved recontacting women in 1989 who had been enrolled in the Nurses Health Study in 1976. They were queried about their spouses' vasectomy status at the time of the initial study. There was no validation of vasectomy status, and only 48% of the reported prostate cancers were confirmed by medical records (15), raising questions about the quality of the exposure and disease information. This same group of investigators analyzed prospective data from the Health Professionals Follow-up Study and found a similar increase in the RR of prostate cancer (RR, 1.6) in relation to vasectomy (16). In the latter study, a total of 422 prostate cancers were self-reported, 417 cases were available for follow-up, and 352 cases (84%) provided consent for medical records that were available to confirm 300 (71%) of the cancers. In addition, information on ever having a DRE was available for 72% of the cohort, which allowed the exclusion of some men who had not had a DRE within the most recent 5-year period. However, no information was available on PSA testing or the frequency of screening for prostate cancer. Interestingly, stratification by stage of disease showed a higher RR for men with localized disease compared to regional/distant stage disease, raising concern about detection bias. If vasectomy status is associated with factors such as health consciousness, access to health care, or screening for prostate cancer, vasectomized men may be overrepresented in the case group. In this situation, failure to account for differences in screening behaviors may result in spuriously elevated risk estimates associated with vasectomy.

Our investigation includes the largest number of middle-aged (<65 years) men with prostate cancer of any study reported to date. Only one other study including 216 cases was limited to men ≤60 years (11). Because vasectomy did not become an accepted method of contraception until the 1960s, the frequency of exposure in our study population was higher than that observed among older men included in the initial studies.

In addition, our study had over 90% power to identify RR estimates of 1.5 or greater (α = 0.05, two-sided test) for the association between vasectomy and prostate cancer. Our results indicate no overall association (OR, 1.1) but suggest that the RR may range from 0.9–1.4. This estimate of effect is compatible with other large population-based case-control studies. For example, John *et al.* (13) reported an OR of 1.1 with an upper 95% CI of 1.3.

It is difficult to draw firm conclusions based on several of the previously conducted studies. This is due to the inconsistency of results across studies, the potential for biases mentioned above, the lack of sufficient power to test the hypothesis, inadequate data to control for prostate cancer screening, and incomplete confirmation of disease status and clinical characteristics. Moreover, in a recent update on the vasectomy-prostate cancer issue, Peterson and Howards (29) emphasize that none of the biological mechanisms proposed as explanations for a possible causal relationship between vasectomy and prostate cancer are either compelling or supported by current basic or clinical research.

The study reported here was specifically designed to address the question of whether or not vasectomy is a risk factor for prostate cancer. Care was taken to obtain additional information in an attempt to overcome some of the limitations of prior investigations. In summary, we found no support for the hypothesis that vasectomy is associated with an increased risk of developing prostate cancer. These findings are particularly noteworthy given the high prevalence of vasectomy and the high incidence of prostate cancer in residents of the geographic area in which this study was conducted. Health care providers, couples considering vasectomy, and men who have undergone vasectomy should find these results reassuring.

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