

Body Size and Prostate Cancer: A Population-based Case-Control Study in China

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Abstract

We conducted a population-based case-control study in China to investigate whether body size plays a role in prostate cancer etiology and whether it can explain the rapid increase in prostate cancer incidence rates in China. A total of 238 cases newly diagnosed with primary prostate cancer in Shanghai, China, during 1993–1995 were included in the study. Four hundred and seventy-one healthy control subjects were randomly selected from among residents of Shanghai and frequency-matched to cases on the basis of age. In-person interviews were conducted to elicit information on height, weight history, and other lifestyle factors. Waist and hip circumferences were measured at interview. Odds ratios (ORs) were used to measure the association between prostate cancer and anthropometric variables including height, weight, body mass index (BMI), waist, hip, and right upper arm circumferences, and waist-to-hip ratio (WHR; an indicator of abdominal adiposity). High levels of WHR were related to an excess risk, with men in the highest quartile ($\text{WHR} > 0.92$) having an almost 3-fold risk (OR, 2.71; 95% CI = 1.66–4.41; $P_{\text{trend}} = 0.0001$) compared with men in the lowest quartile ($\text{WHR} < 0.86$). In contrast, men in the highest quartile of hip circumference (>97.4 cm) had a reduced risk (OR, 0.46; 95% CI = 0.29–0.74; $P_{\text{trend}} = 0.0002$) relative to men in the lowest quartile (<86 cm). No association was found for height, usual adult weight, or preadult and usual adult BMI. Our results suggest that even in a very lean population (average BMI = 21.9), abdominal adiposity may be associated with an increased risk of clinical prostate cancer, pointing to a role of hormones in prostate cancer etiology. Additional research is needed to confirm these

findings in prospective studies, especially in Western populations where abdominal obesity is much more common, and to clarify the underlying hormonal mechanisms involved.

Introduction

Prostate cancer is the most common cancer in Western men (1). It accounts for 23% of all incident cancer cases in men in the United States but for less than 1% of the male cancers in Shanghai, China (2, 3). Incidence rates of clinical prostate cancer in men in the United States are 30–50 times higher than those in Asian men (3, 4). Reasons for the large racial differences in risk are unclear.

Although the reported incidence in Shanghai is one of the lowest in the world, rates are rising rapidly, increasing 70% between 1972–1977 and 1990–1994 (4). Reasons for the rapid increase in prostate cancer incidence in China are unclear. However, screening alone is unlikely to explain the rapidly rising rates in this population because clinical prostate cancer is rare there, and screening is relatively uncommon (4). It is possible that increased westernization and changes in lifestyle may have contributed to some of the rapid rise in incidence.

Westernization has been linked to the increased prevalence of obesity and animal fat intake. Obesity in turn is associated with several hormone-related malignancies and various endocrine and metabolic changes, including lower levels of SHBG² and higher levels of free estradiol (5–7). The role of obesity in prostate cancer, however, is less clear. Results from previous studies have been inconsistent; most reported no association (8–20), and some reported a positive association with BMI (21–26), body weight (27, 28), right upper arm circumference (29), or upper body robustness (*i.e.*, biacromial breadth-to-height ratio and biacromial and bideltoid breadths; Ref 30). One prospective study reported an inverse relationship with obesity at age 21 and a positive association with smaller hips and larger WHR for metastatic cancer (31). Most epidemiological studies to date have focused on adult BMI and few have examined the role of preadult obesity or body fat distribution.

During 1993–1995, we conducted a population-based case-control study in Shanghai, China, to investigate reasons for the extremely low risk of clinical prostate cancer in this population and to identify factors that may help explain the rapid rise in incidence. Using data from this study, herein we report the relationships of obesity as well as body fat distribution with prostate cancer risk.

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²The abbreviations used are: SHBG, sex hormone-binding globulin; BMI, body mass index; OR, odds ratio; CI, confidence interval; WHR, waist-to-hip ratio.

Materials and Methods

Study Population. Details of the study have been described previously (32, 33).³ Briefly, a total of 268 cases of primary prostate cancer (ICD9 185) newly diagnosed between 1993 and 1995 were identified through a rapid-reporting system established between the Shanghai Cancer Institute and 28 collaborating hospitals in urban Shanghai. Cases were permanent residents in 10 urban districts of Shanghai (henceforth referred to as Shanghai) who did not have a history of any other cancer. For cancer cases, a standard medical abstract was used to collect information on date and method of diagnosis. The case ascertainment rate in the study was estimated to be >95% based on the incidence data reported to the Shanghai Cancer Registry.

Information on potential controls was obtained from the personal identification cards maintained at the Shanghai Resident Registry, which contains personal registry cards for all adult residents (>18 years of age) in urban Shanghai. The cards contain name, address, date of birth, gender, and other demographic factors. Those who were deceased, had a history of cancer, or had moved out of the area before the sampling of controls were not eligible for the study. A total of 495 controls were selected randomly from among permanent residents of Shanghai (6.5 million) and frequency-matched to the age distribution (in 5-year age categories) of prostate cancer cases. Study staff visited the home of each selected control to verify his eligibility for the study.

Interview. An in-person interview was conducted to elicit the following information: (a) demographic characteristics; (b) dietary history; (c) consumption of cigarettes and alcohol and other beverages; (d) medical history; (e) family history of cancer; (f) physical activity; (g) body size; and (h) sexual behavior. Cases were interviewed at the hospital, whereas population controls were interviewed at home. Of the 268 eligible cases, 243 (91%) were interviewed. On average, cancer cases were interviewed within 20 days of diagnosis. Of the 495 eligible controls, 471 (95%) were interviewed and 313 (66%) underwent digital rectal examination and prostate-specific antigen testing to identify prostate-related disorders.

Anthropometric Factors. Information on self-reports of adult height, usual adult weight, weight history at various time points in life (at 20–29, 40–49, and 60–69 years of age, and in 1988; hereafter referred to as “the four time points”), perceived body size at the four time points and at 8–9 years of age, maximum adult weight, and the duration of maximum weight were elicited during interview. In addition, after interview, standing height, weight, and circumferences of waist, hip, and right upper arm were measured. Each measurement was taken twice. If the difference between two measurements was larger than a predetermined tolerance (waist, 2.0 cm; hip, 2.0 cm; and right upper arm, 0.8 cm), a third measurement was taken.

Pathology Review. Pathology slides of cases were reviewed by Shanghai study pathologists to confirm the diagnosis and staging of prostate cancer. Subsequently, all pathology slides were reviewed again independently by two pathologists from the Armed Forces Institute of Pathology (I. A. S. and F. K. M.), and a consensus review was held with the Shanghai pathologists to further confirm the diagnosis. After the consensus

Table 1 Selected characteristics of prostate cancer patients and population controls, Shanghai, China

	Cases		Controls	
	n	%	n	%
Total	238	100.0	471	100.0
Age at interview				
<60	10	4.2	10	2.1
60–69	67	28.2	120	25.5
70–79	117	49.2	267	56.7
≥80	44	18.5	74	15.7
Marital status				
Married	214	89.9	440	93.4
Widowed/Separated/Divorced	24	10.1	27	5.7
Never married	0	0.0	4	0.9
Education				
≤Primary school	103	43.3	234	49.7
Junior high	59	24.8	113	24.0
Senior high	40	16.8	68	14.4
≥College	36	15.1	56	11.9
Smoking				
Nonsmokers	100	42.0	174	36.9
Former smokers	64	26.9	121	25.7
Current smokers	74	31.1	176	37.4
Drinking				
Nondrinkers	159	66.8	274	58.2
Former drinkers	35	14.7	36	7.6
Current drinkers	44	18.5	161	34.2
Clinical stage				
Localized	79	33.2		
Regional	74	31.1		
Remote	78	32.8		
Unstaged	7	2.9		
Histological grade				
Well differentiated	22	9.2		
Moderately differentiated	73	30.7		
Poorly differentiated	88	37.0		
Could not be assessed	55	23.1		

review, five cancer cases were determined to have benign prostatic hyperplasia and were excluded from the study, leaving 238 cases for analysis.

Statistical Analysis. ORs and 95% CIs for prostate cancer in relation to anthropometric variables were estimated using multiple logistic regression analysis (34). In the standard model, age at interview, education (none, primary-junior high, ≥senior high), marital status (currently married or other), and total calories were included as potential confounding factors. Total caloric intake was included because it was found to be related to both body size and prostate cancer risk in this study population (the dietary results are reported separately). BMI, expressed as weight divided by the square of height (kg/m^2), was developed as a measure of overall obesity, whereas WHR was used as a measure for abdominal obesity (or upper-body fat). Because waist or hip circumference was related to height and weight, we included BMI in the regression models to estimate the net effect of these two anthropometric factors. In selected analyses, cases were additionally divided into localized and regional/remote categories to evaluate the effect of cancer on these anthropometric factors and to assess whether body size is related to progression of prostate cancer. Smoking, use of alcohol, and other dietary or lifestyle factors were also included in additional analyses.

We derived population-attributable risk estimates for the study population by an approach based on logistic regression (35, 36) to control for age, education, marital status, BMI, and total caloric intake, as was done to estimate ORs.

³ A. W. Hsing, Y.-T. Gao, G. Wu, X. Wang, A. Chokkalingam, J. Deng, J. Cheng, I. A. Sesterhenn, F. K. Mostofi, J. Benchiou, and C. Chang. Polymorphic CAG repeat lengths in the *A1B1* gene and prostate cancer risk: a population-based case-control study in China, submitted for publication.

Table 2 Mean anthropometric characteristics in prostate cancer cases and controls, Shanghai, China

Anthropometric characteristics	Control (n = 471)		Cases					
			Total (n = 238)		Localized (n = 79)		Regional/Remote (n = 150)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Height (cm) ^a	167.5	5.8	167.8	6.1	167.9	5.8	167.8	6.3
Usual adult weight (kg) ^b	61.5	9.7	61.3	8.6	61.2	9.3	61.2	8.2
Measured adult weight (kg) ^c	61.8	10.6	60.4	10.2	61.4	9.8	59.9	10.4
BMI								
20–29 yr	20.4	2.6	20.6	2.5	20.5	2.7	20.6	2.4
40–49 yr	21.8	2.9	21.9	2.8	21.8	2.9	21.9	2.6
60–69 yr	22.2	3.2	22.5	3.4	22.2	3.5	22.7	3.4
Usual adult BMI ^d	21.9	3.1	21.8	2.9	21.7	3.2	21.7	2.6
Measured BMI ^e	22.4	3.4	21.9	3.4	22.3	3.6	21.7	3.2
Measured circumference ^f								
Waist (cm)	82.5	10.5	82.1	10.0	84.1	9.9	80.8	10.0
Hip (cm)	92.5	8.4	90.4	8.6	91.7	8.4	89.5	8.7
Right upper arm (cm)	25.6	3.6	25.1	2.6	25.6	2.6	24.8	2.6
WHR ^g	0.89	0.06	0.91	0.05	0.92	0.05	0.90	0.05

^a Self-reports of usual adult height.

^b Self-reports of usual adult weight.

^c Weight measured at interview.

^d Based on usual adult height and weight (kg/m²).

^e Based on height and weight measured at interview (kg/m²).

^f Measured at interview.

^g Based on measured waist and hip circumferences.

Results

Age at diagnosis ranged from 50 to 94 years (median 73 years) for cancer cases. As shown in Table 1, compared with controls, cases were slightly older, were less likely to be currently married, had a higher level of education, or were less likely to use alcohol. Age, education, and marital status were included in subsequent analyses as covariates. About two-thirds of the cases were diagnosed as having advanced (regional/remote stages) cancer, and most tumors were moderately or poorly differentiated. Most cases were symptomatic at diagnosis, with 77% of the cases having serum prostate-specific antigen levels greater than 10 ng/ml (median levels were 87 ng/ml for total cases, 48 ng/ml for cases with regional cancer, and 205 ng/ml for those with remote cancer).

Table 2 shows the mean anthropometric characteristics in cases and controls. To evaluate the potential disease effect on certain anthropometric factors for cases, results are shown for total cases and separately for localized and advanced cases. Among controls, the mean height and weight were 167.5 cm (65.9 inches) and 61.5 kg (135.3 pounds), respectively, and the average BMI and waist and hip circumferences were 21.9, 82.5 cm (32.4 inches), and 92.5 cm (36.4 inches), respectively. There were no significant differences between groups for height, usual adult weight, measured adult weight (measured at interview), BMI at various ages, usual BMI (based on self-reports of usual adult weight and height), BMI based on weight and height measured at interview, and right upper arm circumference (measured at interview) between cases (all stages) and controls. Cases (all stages), however, had smaller hip circumferences and larger WHRs than controls. Compared with cases with localized cancer, those with advanced cancer (regional/remote) had slightly lower mean levels of measured weight, measured BMI, and measured waist, hip, and right upper arm circumferences but not usual adult weight or usual BMI, suggesting a slight change in body weight among advanced cases. In addition, for these advanced cases, weight measured at interview was slightly lower (2%) than self-report of usual adult

weight. Such a difference, however, was not observed for controls and localized cases.

Because of the possibility of a slight weight loss among advanced prostate cancer, Table 3 presents risk in relation to selected anthropometric characteristics for total cases and by stage of diagnosis. No significant associations were found for height, usual adult weight, or BMI. Increased right upper arm circumference was associated with a reduced risk for advanced cancer.

We examined further the role of body weight and obesity in various decades of life in Table 4. As shown, no strong or consistent risk patterns emerged for reported weight histories or BMI at the four time points. A slight excess risk was associated with a higher BMI in all age groups, although none of the trends was significant. In addition, perceived body size (relative to others in the same age groups) at these four time points plus at age 8–9, maximum weight, duration of maximum weight, and weight changes over time (between 20 and 60 years of age) were evaluated, but no significant associations were found (data not shown).

To investigate further the role of body fat distribution, we examined waist and hip circumferences and WHR (as a measure of abdominal adiposity) in relation to prostate cancer risk (Table 5). The risk patterns for waist circumference were inconsistent, with excess risk found for localized cancer and reduced risk for advanced cancer. In contrast, large hip circumference was associated with a significantly reduced risk, with men in the highest quartile having a 54% reduction in risk (OR, 0.46; 95% CI = 0.29–0.74; $P_{trend} = 0.001$). When the analysis was stratified by stage of cancer, the reduced risks were more pronounced for advanced cancer.

When waist and hip circumferences were considered together (as a ratio), regardless of stage of cancer, high levels of WHR were associated with significant excess risks. For all cases combined, men in the highest quartile of WHR had an almost 3-fold risk (OR, 2.71; 95% CI = 1.66–4.41; $P_{trend} = 0.0001$). When the analysis was further stratified by stage of cancer, much higher risks were observed for localized cancer. Results were materially unchanged when the models were further adjusted for smoking, use of alco-

Table 3 ORs^a and 95% CIs for prostate cancer in relation to selected anthropometric characteristics, Shanghai, China

	Quartiles ^b				<i>P</i> _{trend}
	1	2	3	4	
Height (cm)	<164	164–167	168–171	172–183	
Total prostate cancer	1.00	0.87 (0.55–1.40)	0.68 (0.42–1.09)	1.03 (0.66–1.59)	0.96
Localized prostate cancer	1.00	0.87 (0.42–1.83)	0.78 (0.38–1.62)	1.30 (0.67–2.52)	0.44
Regional/remote prostate cancer	1.00	0.92 (0.53–1.59)	0.65 (0.37–1.14)	0.96 (0.57–1.61)	0.68
Usual adult weight (kg)	<55	55–59	60–64	65–116	
Total prostate cancer	1.00	1.08 (0.63–1.83)	1.15 (0.71–1.87)	1.14 (0.72–1.82)	0.56
Localized cancer	1.00	1.01 (0.45–2.25)	1.17 (0.57–2.42)	1.01 (0.50–2.05)	0.94
Regional/remote prostate cancer	1.00	1.18 (0.63–2.23)	1.17 (0.65–2.08)	1.23 (0.71–2.15)	0.51
BMI (kg/m ²)	<19.8	19.8–21.4	21.5–23.5	23.6–36.1	
Total prostate cancer	1.00	1.12 (0.71–1.76)	0.97 (0.61–1.53)	1.06 (0.67–1.70)	1.00
Localized prostate cancer	1.00	1.16 (0.60–2.23)	0.80 (0.39–1.64)	0.91 (0.45–1.85)	0.57
Regional/remote prostate cancer	1.00	1.05 (0.61–1.81)	1.08 (0.63–1.86)	1.10 (0.63–1.91)	0.73
Right upper arm (cm) ^c	<60.5	60.5–64.8	64.9–70.6	>70.6	
Total prostate cancer	1.00	0.80 (0.51–1.24)	0.96 (0.61–1.50)	0.52 (0.32–0.84)	0.03
Localized prostate cancer	1.00	0.93 (0.46–1.90)	1.14 (0.57–2.27)	0.92 (0.45–1.87)	0.96
Regional/remote prostate cancer	1.00	0.79 (0.47–1.33)	0.93 (0.55–1.55)	0.37 (0.20–0.68)	0.004

^a Adjusted for age, education, marital status, and total calories.

^b Based on the distribution among 471 controls. Numbers in parentheses, 95% CI.

^c Measured at interview.

Table 4 ORs^a and 95% CIs for prostate cancer in relation to histories of weight and BMI at four time points in life, Shanghai, China

	Quartiles ^b				<i>P</i> _{trend}
	1	2	3	4	
Weight (kg) ^c					
20–29 yr	1.00	1.06 (0.67–1.69)	1.11 (0.69–1.80)	1.04 (0.65–1.67)	0.87
40–49 yr	1.00	1.08 (0.63–1.83)	0.96 (0.60–1.53)	1.07 (0.65–1.77)	0.92
60–69 yr	1.00	0.92 (0.52–1.62)	1.24 (0.77–2.00)	1.51 (0.92–2.48)	0.04
In 1988	1.00	1.05 (0.61–1.79)	1.08 (0.68–1.71)	1.26 (0.78–2.03)	0.78
BMI (kg/m ²) ^d					
20–29 yr	1.00	2.11 (1.28–3.46)	1.51 (0.90–2.53)	1.59 (0.95–2.66)	0.30
40–49 yr	1.00	1.07 (0.67–1.37)	1.20 (0.75–1.91)	1.14 (0.70–1.84)	0.51
60–69 yr	1.00	1.24 (0.77–2.00)	1.36 (0.84–2.20)	1.28 (0.79–2.06)	0.31
In 1988	1.00	1.07 (0.67–1.70)	1.20 (0.75–1.91)	1.15 (0.73–1.83)	0.48

^a Adjusted for age, education, marital status, and total calories.

^b Based on the distribution among controls. Numbers in parentheses, 95% CI.

^c Self-reports of weight in kg. Cutoffs for quartile were: 20–29 years: <52, 52–60, 61–65, >65; 40–49 years: <55, 55–60, 61–66, >66; 60–69 years: <55, 55–60, 61–66, >66; in 1988: <55, 56–60, 61–68, >68.

^d Self-reports of BMI. Cutoffs for quartile were: 20–29 years: <18.59, 18.60–20.20, 20.21–21.97, >21.97; 40–49 years: <19.82, 19.83–21.48, 21.49–23.51, >23.51; 60–69 years: <19.82, 19.82–21.97, 21.98–24.17, >24.17; in 1988: <19.82, 19.82–21.80, 21.81–24.03, >24.03.

hol, physical activity, benign prostatic hyperplasia, diabetes, or selected dietary factors (consumption of red meat and protein; data not shown).

Table 6 presents prostate cancer risks in relation to WHR and BMI. In the first model, using tertiles of BMI and WHR as the cutoffs, increasing levels of WHR were associated with an elevated risk of prostate cancer, regardless of levels of BMI. The excess risk was more pronounced among men in the first (<20.5) and second (20.5–22.8) tertile of BMI. In addition, the excess risk associated with WHR was much less evident among those with a BMI >25. Within the same level of WHR, increases in BMI had a relatively small impact on risk.

Discussion

Our population-based case-control study revealed that higher levels of WHR and a smaller hip circumference, but not BMI, body weight, or height, were significant risk factors for clinically overt prostate cancer in China. These results suggest that even in a very lean population (average BMI = 21.9), body fat

distribution rather than overall obesity may play a role in prostate cancer etiology.

BMI, reflecting both lean and fat body mass, is the most common measure of overall adiposity. Although eight studies did report a positive association between BMI and prostate cancer (20–26), most epidemiological studies have not found significant effects for BMI and prostate cancer (7–20, 27–30). We too did not find BMI to be associated with prostate cancer risk. We may not be able to evaluate the effect of overall obesity fully, inasmuch as only 4% of our study subjects were considered overweight (BMI >27.8) versus 24% in men in the United States (37, 38). BMIs in our study subjects ranged from 19.8 to 35.1, with an average of 21.9, which was even smaller than the cutoff point for the baseline category (BMI <23) in a prospective study of United States health professionals (31).

Several studies have reported that body weight at birth or BMI at an early age was related to an excess prostate cancer risk, especially for advanced disease (39–41). We evaluated the role of obesity in early life by examining BMI at four time

Table 5 ORs^a and 95% CIs for prostate cancer in relation to waist and hip circumferences and WHR, Shanghai, China

	Quartiles ^b				<i>P</i> _{trend}	
	1	2	3	4		
Waist circumference (cm) ^c	<75	75–82.3	82.4–89.3	89.4–115.0		
Total prostate cancer	1.00	1.27	(0.80–2.00) ^d	1.20	(0.77–1.89)	0.63
Localized prostate cancer	1.00	1.90	(0.88–4.07)	1.97	(0.92–4.18)	0.19
Regional/remote prostate cancer	1.00	1.05	(0.62–1.75)	0.93	(0.56–1.55)	0.07
Hip circumference (cm) ^c	<86.0	86.1–91.9	92.0–97.3	97.4–122.8		
Total prostate cancer	1.00	0.53	(0.34–0.83)	0.53	(0.34–0.83)	0.001
Localized prostate cancer	1.00	0.42	(0.20–0.88)	0.80	(0.42–1.53)	0.41
Regional/remote prostate cancer	1.00	0.55	(0.33–0.91)	0.40	(0.23–0.69)	0.0002
WHR ^e	<0.86	0.87–0.89	0.90–0.92	0.93–1.12		
Total prostate cancer	1.00	1.23	(0.72–2.10)	2.15	(1.31–3.52)	0.0001
Localized prostate cancer	1.00	1.23	(0.49–3.13)	2.68	(1.17–6.16)	0.0001
Regional/remote prostate cancer	1.00	1.28	(0.70–2.36)	1.98	(1.12–3.52)	0.0036

^a Adjusted for age, education, marital status, total calories, and BMI.

^b Based on the distribution among 471 controls.

^c Measured at interview.

^d 95% CIs.

^e Based on waist and hip circumference measured at interview.

Table 6 ORs^a and 95% CIs for prostate cancer in relation to BMI and WHR, Shanghai, China

WHR ^b	BMI								
	<20.5 ^c			20.5–22.8			>22.8		
	N1/N2 ^d	OR	95% CI	N1/N2	OR	95% CI	N1/N2	OR	95% CI
<0.87	(21/69)	1.00		(13/50)	0.80	(0.36–1.76)	(9/35)	0.78	(0.32–1.90)
0.87–0.90	(31/53)	1.91	(0.98–3.72)	(29/57)	1.67	(0.85–3.26)	(19/44)	1.41	(0.67–2.94)
>0.90	(26/33)	2.49	(1.22–5.10)	(33/48)	2.12	(1.08–4.13)	(50/78)	1.96	(1.06–3.63)
	<21.0 ^c			21.0–25.0			>25.0		
<0.87	(25/85)	1.00		(14/57)	0.80	(0.38–1.69)	(4/12)	1.16	(0.34–3.95)
0.87–0.90	(37/72)	1.78	(0.98–3.25)	(35/67)	1.83	(0.99–3.38)	(7/15)	1.59	(0.58–4.40)
>0.90	(34/39)	2.92	(1.53–5.58)	(56/79)	2.29	(1.29–4.04)	(19/41)	1.54	(0.76–3.16)

^a Adjusted for age, education, marital status, total calories, and BMI.

^b Based on measured waist and hip circumferences at interview. Tertile levels among controls were used as the cutoffs.

^c Based on self-report of usual adult height and weight at interview (kg/m²). Tertile levels among controls were used as the cutoffs.

^d Number of cases (N₁) and controls (N₂).

^e Arbitrary cutoffs.

points (using self-reports of height and weight at these time points) and self-perceived body size at these four time points and at age 8–9, but we were unable to confirm the hypothesis that preadult obesity was associated with an inverse risk (31). In fact, in our study, BMI in later years (60–69 years of age) was associated with higher risk than that at younger ages (20–29 or 40–49 years of age). Although long-term recall of past weight is difficult, several validation studies conducted in Western men have reported a high reproducibility of self-reports of past weight and high correlations between recall of recorded and past weight (42–44). In our study, self-reports of body height, usual adult weight, and weight in both 1988 and at 60–69 years of age were similar to measurements taken at interview, suggesting some level of consistency in the recall of body weight among Chinese men. In addition, among the 471 controls, values for BMI at various time points in life correlated well with each other.

Few studies have investigated the role of body fat distribution in prostate cancer. Despite the very low prevalence (4%) of overall obesity in our study subjects, we found that, independent of BMI, a greater WHR is an important risk factor for prostate cancer. When the analysis was further stratified by BMI, higher levels of WHR, but not BMI, were strongly related to risk. The risk associated with WHR was more pronounced among men with a low

level of BMI (<25), suggesting that lean people with upper-body fat may be at greater risk of prostate cancer. We did not have enough obese subjects in the study to evaluate fully the effect of abdominal adiposity among obese subjects and the combined effect of abdominal and overall obesity.

In one prospective study among men in the United States, higher levels of WHR and smaller hips were associated with an increased risk of metastatic prostate cancer (31), trends were not statistically significant. Relative to our study subjects, these Western men had much higher levels of BMI and WHR. In our study, 4% of the study subjects were considered overweight (BMI >27.8) versus 25% of the Western subjects, and 26% were considered to have abdominal obesity with a WHR >0.92 (versus 60% in men in the United States; Ref. 31). For both waist and hip circumferences, cutoff points for the highest quartile (75th percentile) in our study were similar to those for the 40th percentile in Western men (31).

The WHR is a standard measure for abdominal adiposity, which has been linked to hormonal changes, metabolic aberrations (such as insulin resistance, glucose intolerance, hyperinsulinemia, and hyperlipidemia), and certain morbidities, including diabetes mellitus, cardiovascular disease, and cancers of the breast and endometrium (45, 46). In men, abdominal obesity is associated

with higher circulating levels of cortisol, insulin, leptin, and free fatty acids but with lower levels of free testosterone and SHBG (47–51), although the precise hormonal mechanism is unclear. The WHR is a measure of both visceral and subcutaneous fat; most of the metabolic changes are linked more closely to visceral fat in the intra-abdominal area. We have no data on visceral fat. Future studies are needed to confirm the finding regarding upper-body fat and to elucidate further the role of visceral fat. Whether WHR among lean subjects better reflects hormonal status also needs to be investigated further.

It has been suggested that waist circumference alone is also a good indicator of abdominal obesity and perhaps a better predictor of cardiovascular risk than WHR. In our study, however, the association with waist circumference was less consistent. Large waist circumference was associated with a nonsignificant increased risk of localized prostate cancer. However, the reduced risk for advanced cases associated with a large waist may be attributable, in part, to minor weight loss in advanced cases. On the basis of self-reported usual adult weight and measured weight at interview, we estimated that, on average, cases with advanced cancer may have lost up to 2.9 pounds, with two cases and three controls reporting a weight loss of more than 5 pounds. Exclusion of subjects with weight loss more than 2 pounds did not materially change the results. The minor weight loss in cases with advanced tumors might have resulted in their smaller measured circumferences of waist, hip, and right upper arm (0.3–1.3 inches smaller than those for men with localized cancer). Previous data suggest that among men, weight loss could result in more reduction in waist than in hip circumference (52), resulting in a lower WHR. Thus, weight loss in cases with advanced tumors, but not in controls, should lead to lower WHRs in cases and result in an underestimate of the true risk. The risk estimates for localized cancer were higher than those for advanced cancer, suggesting that the overall risks for all cases combined may have been even higher than those reported here.

Hip circumference reflects gluteo-femoral adipose tissue, a major component of peripheral obesity. We found that larger hips were associated with a reduced risk of prostate cancer independent of WHR. This inverse relationship has been reported previously (31), and an earlier clinical study reported an inverse correlation between free testosterone and larger hips (53). Because of small numbers and the high correlation between waist and hip circumference ($r = 0.7$), we were unable to evaluate the role of hip circumference independent of abdominal adiposity. Because WHR is a ratio estimator, in an additional analysis, we included both WHR and hip circumference in the same model, and results were materially unchanged. Additional studies are needed to elucidate the independent protective effect of large hips on prostate cancer.

Of all of the lifestyle factors examined in the study to date, WHR is the strongest, with the most consistent patterns and dose-response relationship. The strong and consistent dose-response relationship suggests that the observed association may be real. Future studies are needed to confirm this association, especially in prospective studies in which the anthropometric measurements are taken before the diagnosis of disease and in Western populations where the risk of prostate cancer and the prevalence of abdominal obesity are much higher. International trends in prostate cancer suggest that westernization may increase the risk of prostate cancer (4). Westernization in developing countries is related to an improved socioeconomic status, an increase in animal fat and red meat intake, reduced levels of physical activity, and an increase in the incidence of obesity and diabetes mellitus. Most of these factors have been linked to higher WHRs (54). However, the observed WHR association in this study is inde-

pendent of socioeconomic status, overall obesity, physical activity, intake of animal fat and red meat, and total calories. Although possible, it is unlikely that some unknown factors related to westernization may be confounding the observed association.

It has been shown that lean muscle mass, but not fat mass, in the arm area was associated with testosterone and an increased risk of prostate cancer in a prospective study among Japanese-American men (29). In our study, we found that larger right upper arm circumference was associated with a reduced risk of advanced cancer even after adjustment for BMI or WHR. This result needs to be interpreted with caution, because such a reduction in risk was found only for advanced cancer but not for localized cancer, suggesting that the reduced circumference related to weight loss among cases with advanced cancer could have potentially biased the results. Right upper arm circumference in our study correlated strongly and positively with hip circumference (more than with waist circumference and WHR), and when the model was further adjusted for hip circumference, the ORs were >1 . The arm circumference in our study reflects both fat and lean muscle mass; we have no information on lean muscle mass in the arm area.

Adult height has been reported in several studies to be associated with an increased prostate cancer risk (13, 17, 19, 31, 55, 56). In a recent study showing a positive association with height, substantial risk (22–68% excess) was found only for men who were taller than 72 inches (56). We were unable to evaluate the risk in relation to height fully, because the variation in height is limited and because very few study subjects (2%) were taller than 72 inches. In our study, men in the highest quartile were only taller than 172 cm (67.7 inches), which is usually the baseline group in Western studies.

In summary, our findings suggest that abdominal adiposity, especially among nonobese men, is a strong risk factor for prostate cancer. Assuming that the abdominal adiposity association is causal, we estimated that 24% (95% CI = 14–33%) of the cases in Shanghai can be attributed to abdominal obesity (WHR > 0.92). Additional research is needed to confirm this finding in Western populations, where the prevalence of abdominal obesity is much higher, and to clarify the underlying hormonal mechanisms involved.

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