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Prostate Cancer Risk Reduced by Physical Activity Even Among Men With Prolonged Sitting Time: A Study From Vietnam

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Abstract

Increasing prostate cancer incidence in the Asia-Pacific region may be related to a more sedentary lifestyle resulted from economic growth and rapid urbanization. The present case-control study of 640 men aged 64 to 75 years was conducted in Vietnam between 2013 and 2015 to ascertain the relationship between physical activity and prostate cancer risk, accounting for the duration of sitting time. Reduced prostate cancer risks were found for men engaging in medium (15.8-47.3 metabolic equivalent task [MET]-h/week) and high (>47.3 MET-h/week) physical activity levels, with the adjusted odds ratios being 0.52 (95% confidence interval = 0.35-0.77) and 0.27 (95% confidence interval = 0.14-0.49), respectively. This association was independent of sitting time. Analyses of joint association of physical activity and sitting time also found a reduction in the cancer risk for higher energy expenditure levels. Similar results were evident for both low-medium and high grade tumors. The findings are important for developing health strategies to prevent prostate cancer in Asian countries.

Keywords

prostate cancer, Vietnam, physical activity, sitting time, case-control study

Introduction

Prostate cancer (PCa) is a leading cause of cancer-related deaths, and one of the most common malignancies in men.[1] Historically, its incidence rate was relatively low (<20 per 100 000 age adjusted) in developing countries, but has been increasing in the past few decades, making PCa an emerging public health issue in the Asia-Pacific region.[2] This increase is associated with changing lifestyle and diet in the region.

Sedentary behavior is defined as activities, such as sitting or lying, with energy expenditures less than 1.5 metabolic equivalent tasks (METs).[3] Increasing urbanization and industrialization has led to a more sedentary lifestyle.[4-6] There is evidence suggesting that prolonged sitting time

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(ST) can increase the risks of colon, endometrial, and lung cancers,[7] but the relationship between ST and PCa remains unclear.[8] In contrast, higher levels of physical activity (PA) appear to be associated with a reduced risk of PCa.[9] A meta-analysis of 19 cohort and 24 case-control studies found a pooled relative PCa risk of 0.90 (95% confidence interval = 0.84-0.95), but with some inconsistencies between Canadian, Asia-Pacific, American, and European populations.[10] ST may also be independently associated with an increased risk of PCa.[11] It is thus important to investigate whether prolonged ST can attenuate the protective effect of PA against PCa.

In Vietnam, a recent survey showed that about 30% of men did not meet the PA recommendations of the World Health Organization, especially in urban areas (~50%).[12] A cohort study of nonschool adolescents found that sedentary behavior has become more prevalent in recent years.[13] Given the upward trend of PCa incidence in Vietnam over the past decade,[14] practical recommendations for prevention are needed. The aim of this study was to investigate the joint effect of PA and ST on the risk of developing PCa in Vietnam.

Methods

Study Design and Participant Recruitment

A case-control study was conducted in Ho Chi Minh City, Vietnam, between January 2013 and July 2015. Cases were incident PCa patients, aged 64 to 75 years, and only those with histological confirmation within 1 week prior to their interview were included. Cases with any history of malignancy or severe chronic diseases (eg, diabetes and stroke), or without consent to participate in the study, were excluded. A total of 272 confirmed cases were approached, but 19 declined to participate, resulting in 253 PCa patients being recruited and interviewed. Furthermore, 22 patients were later excluded due to either missing or illogical information, leaving 231 cases available for subsequent analysis.

Controls were men who either attended the same hospitals for a health examination or were residing in the same catchment area as the cases. They were frequency-matched to the cases by 5-year age groups. Of the 700 community-dwelling older men aged 64 to 75 years who we contacted, 429 consented to take part in the study. After an initial screening, 62 men were excluded for the following reasons: (1) having malignant or severe chronic diseases, (2) refusal to undertake a prostate-specific antigen (PSA) test, or (3) having serum PSA level exceeded 4 ng/mL. As a result, 367 eligible men attended the interview with their written consent (response rate = 52.4%). In addition, we approached 120 eligible patients who attended the same hospitals (as the cases) for minor treatment or health check. A total of 83 outpatients gave their consent for the interview (response rate = 69.1%). The process of data cleansing further excluded 27 community-based controls and 14 hospital-based controls due to their illogical or missing information. The final sample consisted of 409 controls (340 community-based and 69 hospital-based) and 231 cases.

Data Collection

Information about PA, ST, and other variables were collected through face-to-face interview using a structured questionnaire. A signed consent form was obtained before each interview, which took about 40 minutes to complete. During the interview the presence of the participant's next-of-kin was encouraged to maximize the accuracy of information collected. Both interviewers and participants were blinded to the study hypothesis.

Exposure measurements included demographic and lifestyle characteristics (eg, age, marital status, education level, and smoking), medical history (including histological examination and PSA level), height, weight, and dietary habits (using a food frequency questionnaire to estimate total energy intake). PA and ST questions were taken from those used in previous studies of older

adults,[15,16] which included validated components from the Hawaii Cancer Research Survey[17] and the Australian Health Survey 1995.[18] Participants were asked to report the number of hours they engaged in different levels of PA per week, dating back 3 years before the interview, on (1) strenuous sports including jogging, bicycling on hills, tennis, racquet ball, swimming, and aerobics; (2) vigorous work such as moving heavy furniture, shoveling, weight lifting, loading/unloading trucks, or equivalent manual labor; and (3) moderate activities such as housework, brisk walking, golfing, bowling, bicycling on level ground, gardening, and tai chi. Total ST comprising sitting time (hours) at home, work, travel, watching television, eating meals, reading, listening to radio, playing cards, or computer games was also estimated using the questionnaire.

Statistical Analysis

The demographic and lifestyle characteristics of the case and control groups, especially PA and ST levels, were compared using χ^2 test, 2-sample t test, and Wilcoxon rank-sum tests. Total PA was the sum of all types of PA expressed in terms of MET-h/week. Data from the Compendium of PA[19] were used to compile the MET values, with intensity codes 8.5, 6.0, and 4.5 MET being assigned to strenuous sports, vigorous work, and moderate activities, respectively.

To examine their association with the PCa risk, the continuous PA and ST variables were categorized into 3 levels (low, medium, high), using tertiles of the corresponding control distribution as the cutoff points. The lowest levels were then taken as the reference group in separate unconditional logistic regression models.

To determine whether ST could attenuate the association between PA and the risk of PCa, total PA and ST were dichotomized into high and low levels according to the median among controls, namely, 31.5 MET-h/week and 53.5 h/week. They were then combined to form 4 intensity categories, specifically, low PA-high ST, low PA-low ST, high PA-high ST, and high PA-low ST. The low PA-high ST was regarded as the reference category representing the lowest level of energy expenditure.

Adjusted odds ratios and associated 95% confidence intervals were presented, and tests for linear trend were performed to assess the apparent dose-response relationships. The multivariable logistic regression models accounted for potential confounding factors, namely, age at interview (years), age at marriage (years), body mass index (kg/m^2), alcohol consumption (g/day), total energy intake (kcal/day), education level (primary, high school, tertiary), marital status (never married or separated, married), smoking habit (never, former, current), and PCa in the first-degree relatives (yes, no). These variables were either established or plausible risk factors from the literature. Finally, cases were classified as either low-medium (Gleason score ≤7) or high (Gleason score 8-10) grade PCa[20] for subgroup analysis. All statistical analyses were performed using the R statistical software version 3.3.3.[21] An observed $P < .05$ was considered statistically significant.

Results

As shown in Table 1, the age of participants was about 69 years. Compared with controls, the PCa patients were married at a younger age, drank more alcohol, and had significantly less energy intake before diagnosis. The 2 groups were also different in terms of educational level, moderate PA level, and total PA level, with the cases being less educated and less active than their control counterparts. First-degree family history of PCa was reported by 7 cases only.

The results of multivariable logistic regression analyses, presented in Table 2, showed that increasing levels of PA were significantly associated with a lower risk of PCa ($P_{trend} < .01$). On the other hand, prolonged ST appeared to raise the PCa risk marginally, though not statistically significant ($P_{trend} = .27$). No interaction was apparent between PA and ST (adjusted odds ratio = 0.69; 95% confidence interval = 0.27-1.75; $P = .44$).

Table 1. Sample Characteristics of Vietnamese Men by Case-Control Status.

Characteristic	Controls (N = 409)	Cases (N = 231)	P^a
Age (years), mean ± SD	67.9 ± 5.9	68.8 ± 7.2	.11
Age at marriage (years), mean ± SD	27.3 ± 4.9	25.1 ± 4.9	<.001
Body mass index (kg/m^2), mean ± SD	21.9 ± 3.3	22 ± 3	.93
Alcohol consumption (g/day), mean ± SD	15.4 ± 30.2	23 ± 48.3	.03
Total energy (kcal/day), mean ± SD	1940 ± 720	1623 ± 647	<.001
Education level, n (%)			
Primary school	71 (17.4)	58 (25.1)	.04
High school	264 (64.5)	129 (55.8)	
Tertiary	74 (18.1)	44 (19.1)	
Marital status, n (%)			.09
Never married or separated	33 (8.1)	10 (4.3)	
Married	376 (91.9)	221 (95.7)	
Smoking habit, n (%)			
Never	111 (27.1)	55 (23.8)	.16
Former	170 (41.6)	114 (49.4)	
Current	128 (31.3)	62 (26.8)	
Prostate cancer in the first-degree relatives, n (%)	0 (0)	7 (3)	—
Strenuous sport (yes), n (%)	8 (2)	3 (1.3)	.76
Vigorous work (yes), n (%)	12 (2.9)	6 (2.6)	1
Moderate physical activity (h/week)			
Mean ± SD	6.3 ± 5.1	4.5 ± 3.8	<.001
Total physical activity (MET-h/week)			
Mean ± SD	33 ± 24.6	21.6 ± 18.3	<.001
Sitting time (h/week)			
Mean ± SD	54.3 ± 12.1	54.2 ± 13.1	.77

Abbreviations: SD, standard deviation; MET, metabolic equivalent task.
[a]*P*-value from *t* test, Wilcoxon rank-sum test, or χ^2 test.

Table 2. Adjusted Odds Ratios and Associated 95% Confidence Intervals of Prostate Cancer Risk for Total Physical Activity and Sitting Time[a].

	Control (N = 409)	Case (N = 231)	Odds Ratio[a]	95% Confidence Interval
Total physical activity (MET-h/week)				
15.8	141 (34.5)	136 (58.9)	1	Reference
15.8-47.3	182 (44.5)	77 (33.3)	0.52	0.35-0.77
>47.3	86 (21.0)	18 (7.8)	0.27	0.14-0.49
				$P_{trend} < .01$
Sitting time (h/week)				
<45.5	108 (26.4)	60 (25.9)	1	Reference
45.5-62.0	199 (48.7)	102 (44.2)	1.03	0.66-1.62
>62.0	102 (24.9)	69 (29.9)	1.40	0.85-2.31
				$P_{trend} = .27$

Abbreviation: MET, metabolic equivalent task.
[a]Adjusted for age at interview (years), age at marriage (years), body mass index (kg/m^2), alcohol consumption (g/day), total energy intake (kcal/day), education level (primary school, high school, tertiary), marital status (never married or separated, married), smoking habit (never, former, current), and prostate cancer in the first-degree relatives (yes, no).

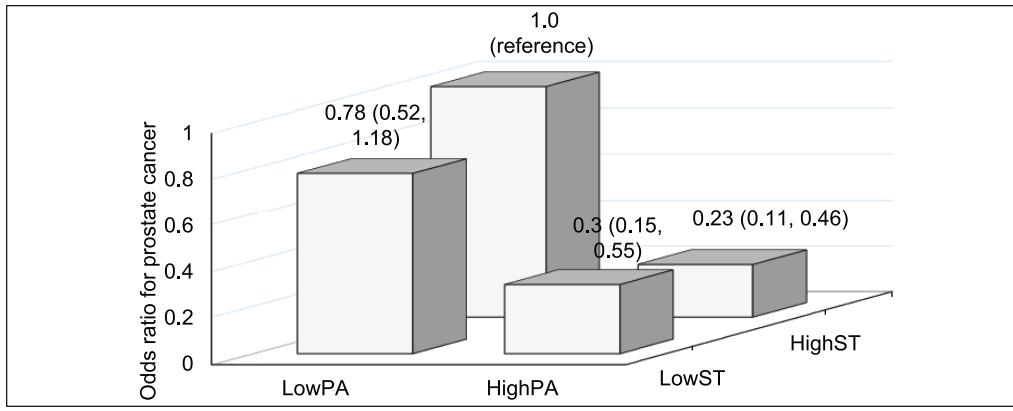

Figure 1. Adjusted odds ratios and associated 95% confidence intervals of prostate cancer risk for joint effect of physical activity (PA) and sitting time (ST).
PA and ST were dichotomized into high and low levels according to the median among controls; odds ratios were adjusted for age at interview (years), age at marriage (years), body mass index (kg/m^2), alcohol consumption (g/day), total energy intake (kcal/day), education level (primary school, high school, tertiary), marital status (never married or separated, married), smoking habit (never, former, current), and prostate cancer in the first-degree relatives (yes, no).

The joint effects of PA and ST was next examined. The results, presented in Figure 1, suggested that the inverse association between PA and PCa risk was not attenuated or modified in any way by ST, where a significant lower risk was evident for men with high PA regardless of their ST duration. Such inverse associations persisted for both low-medium and high grade PCa (results available on request). Similarly, no significant interaction between PA and ST was observed for both low and high grades of PCa.

Discussion

This case-control study investigated the joint association between PA, ST, and the risk of PCa. Logistic regression and subgroup analyses confirmed that the inverse association between PA and the PCa risk was not attenuated by ST in Vietnamese men.

In the literature, relatively little attention had been paid to the role of ST.[10] Several studies reported that the effect of ST was independent of PA,[8,22] consistent with studies in breast cancer[11] and colorectal cancer.[23] The present study provided the first epidemiological evidence that ST does not attenuate the effect of PA against the development of PCa. Our findings suggested that regardless of the duration of ST, being physically active may still be able to reduce the PCa risk. Similarly, it has been reported that ST and PA acted independently in terms of influencing health-related quality of life among PCa patients.[24]

The mechanism by which PA and ST affect the development of PCa remains unclear. Despite some interrelation between PA and ST with regard to biological pathway of PCa carcinogenesis,[9,25] they appear to be distinct from each other.[3] For example, PA is inversely associated with circulating levels of insulin-like growth factors and testosterone,[9] which are believed to reduce the stimulation to the growth and proliferation of neoplastic cells.[26-28] On the other hand, ST is not associated with sex hormones.[25] This difference may partly explain their independent effects on the PCa risk. However, ST is associated with obesity, metabolic dysfunction, and chronic inflammation, processes that may play an operative role in carcinogenesis,[25] and may facilitate PCa development and progression.[29,30] Indeed, ST has been reported to increase the risk of colon, endometrial, and lung cancers.[7]

In this study, we adopted the same approach as previous cancer epidemiology studies, namely, the use of questionnaire to assess habitual PA and ST exposure before cancer diagnosis.[9,15,16] Other methods, such as exercise log book and objective measurements (eg, from pedometer or accelerometer), are inappropriate because they can only measure current PA levels after cancer diagnosis. However, we did not validate the PA questionnaire in the Vietnamese elderly population, which was beyond the scope of the present study.

The interpretation of the results should take account of several limitations. First, PA generally decreases with age; therefore, we focused on the moderate activity of the elderly participants. Second, despite the potential for incurring recall error, we set a reference recall period of 3 years before the interview for both case and control groups. The purpose was to avoid possible change in PA exposure since the disease onset (for cases), and to reflect habitual activities of controls. Third, recall bias might occur if cases recalled their history of participation in PA differently from the controls. To minimize such bias and to improve the accuracy of information obtained, the same trained interviewers were used to conduct the face-to-face interviews following an identical protocol for both case and control groups in the presence of their next-of-kin. Finally, information bias seemed to be minimal since PCa was low incident in Vietnam, and little attention has been paid to PA at the time of conducting the study. Residual confounding might still be a possibility, even though the effects of potential confounders have been accounted for in the logistic regression analyses.

Conclusion

Being physically active was associated with a reduced risk of PCa for Vietnamese men. This inverse association was significant regardless of the tumor grade and was not attenuated by prolonged ST.

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Ethical Approval

This study was approved by the Human Research Ethics Committee of Curtin University (Approval Number: HR 109/2012). Recruitment and access to medical records were permitted by the participating hospitals and local commune health centers.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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