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Trichomonas vaginalis infection and risk of advanced prostate cancer

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Abstract

Background—The epidemiologic evidence for an association of *Trichomonas vaginalis (Tv)* with overall prostate cancer is mixed, but some studies suggest *Tv* may increase risk of more agressive disease. The aim of this study was to assess whether *Tv* serostatus is associated with advanced or fatal prostate cancer.

Methods—146 men with advanced (metastatic or fatal) prostate cancer and 181 age-matched controls were selected from two prior population-based, case-control studies. *Tv* serostatus was determined with the same laboratory methods used in previous epidemiologic studies. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using multivariable logistic regression to compare *Tv* serostatus in prostate cancer cases and controls adjusted for potential confounders.

Results—The seroprevalence of *Tv* in controls was 23%. *Tv* serostatus was not associated with an increased risk of metastatic or fatal prostate cancer (ORs<1).

Conclusions—Our study does not support an increased risk of advanced or fatal prostate cancer in men seropositive for *Tv*.

Introduction

Trichomonas vaginalis (Tv) is a relatively common parasitic sexually transmitted infection. The majority of infections are non-symptomatic in men and remain undiagnosed and untreated, which has been hypothesized to result in chronic persistent prostatic infection[1].

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Cell line studies found that *Tv* provokes an inflammatory response in prostate epithelial cells,[1] and a *Tv* secreted macrophage inhibitory factor increased prostate cell proliferation and invasiveness and induced cellular pathways linked to inflammation[2]. As such, persistent *Tv* infection in the prostate may result in a tumor promoting pro-inflammatory microenvironment. The epidemiologic evidence for an association of *Tv* and prostate cancer (PCa) is mixed, but possibly suggestive of an association with advanced PCa[3-5]. The aim of this study was to assess whether *Tv* serosatatus is associated with an increased risk of advanced or fatal PCa.

Materials and Methods

PCa cases and controls were selected from participants enrolled in prior population-based case-control studies previously described[6,7]. We included 146 men with advanced (metastatic or fatal) PCa and 181 age-matched controls. Given alpha=0.05 and 23% *Tv* seroprevalence in controls, our study had 80% power to detect an OR of approximately 2.0, which is within the range of risk estimates reported by prior studies. Blood samples were collected during an in-person interview, kept on ice, processed within 4-6 hours using standard protocols, and stored at −80°C. The median time from PCa diagnosis to blood draw was nine months.

Tv serostatus was determined as in previous epidemiologic studies[3-5] in the Alderete laboratory[8]. Cases and controls were plated randomly across ten plates and laboratory technicians were blinded to case-control status. The serostatus concordance of ten blinded quality control duplicate samples was 90%, and concordance of two blinded technical replicates on each of the ten plates was 80% and 70%; these measures are comparable to those in other published studies[3-5].

Odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression to compare *Tv* serostatus in PCa cases and controls, adjusted for age at reference date, study, race (African American, Caucasian), PCa screening history in the 5 years prior (digital rectal exam, PSA test), and smoking status (current, former, never).

Results

Table 1 describes study population characteristics by *Tv* serostatus in controls and by disease status. The mean age at PCa diagnosis was 58.8 years. The prevalence of Tv seropositivity was 23% in controls. *Tv* seropositive controls were less likely to have a PCa screening history and more likely to be smokers and African American. Cases were less likely to have a screening history and more likely to be smokers, African American, and have family history of PCa. We did not observe increased risk estimates for advanced or fatal PCa in *Tv* seropositive men (**Table 2**). In fact, the point estimates were in the protective direction; seropositive men had a non-statistically significant decreased risk of fatal PCa (OR: 0.57; 95% CI: 0.30-1.08) and a statistically significant decreased risk of advanced PCa (OR: 0.51; 95% CI: 0.28-0.93) in the fully-adjusted models. These results were attenuated when we restricted the analysis to Caucasian men. There were not enough African American men for a subgroup analysis (16 cases and 14 controls).

Discussion

To date, three published epidemiologic studies have investigated *Tv* and PCa risk using plasma antibodies to define infection history status. One study found no association for early-stage disease[5] and two found an increased risk of PCa, especially more aggressive disease[3,4]. Only one study assessed metastatic and fatal PCa (n=139) and found an increased risk in seropositive men[3]. In our population-based study, we did not observe an increased risk of metastatic and fatal prostate cancer (n=146) among seropositive men. Moreover, the point estimates of risk suggest an inverse association. Similarly, Sutcliffe et al.[5] did not find an increased risk of PCa in relation to *Tv* seropositivity, and the risk estimate for high-grade cancer was in the inverse direction; that study did not assess advanced stage or fatal PCa.

One difference in the design of our study compared to those previously published is that our samples were collected after diagnosis. Although a possibility, reverse causation is unlikely to completely explain our findings as there is no direct evidence that PCa or its treatment would result in lower detection of *Tv* antibodies. Moreover, a previous study found a stronger positive association of *Tv* with advanced PCa in men whose blood was collected closer to diagnosis[3]. Residual confounding by unhealthy behaviors (e.g. smoking) is also unlikely to explain our results as we would expect the bias to go in the opposite direction of our observed findings. Finally, misclassification of serostatus is likely to be nondifferential with respect to case control status and could bias our results towards the null. In conclusion, our study results do not support a positive association between *Tv* and advanced or fatal PCa.

Acknowledgments

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Table 1

Characteristics of the study population by *T. vaginalis (Tv)* serostatus in controls and by case-control status.

	Controls only		Cases vs. controls	
	***Tv* negative (n=139)**	***Tv* positive (n=42)**	**Cases (n=146)**	**Controls (n=181)**
Characteristics				
Age at reference date* (years), mean (std)	58.8 (7.4)	59.6 (6.5)	58.8 (7.4)	59.0 (7.2)
Family history of prostate cancer, %	11	10	14	11
Race, %				
Caucasian	94	86	89	92
African American	6	14	11	8
Prostate cancer screening history#, %				
Yes	90	83	77	88
Number of lifetime female sexual partners^, %				
1	28	26	18	28
2 to 4	23	21	27	22
5 to 14	25	29	30	26
≥15	25	24	26	24
Smoking status, %				
Current	13	19	19	14
Former	41	48	49	43
Never	46	33	32	43
BMI (kg/m2), mean (std)	27.1 (3.7)	27.2 (3.8)	27.1 (4.1)	27.1 (3.7)

*Date of diagnosis for cases and similar assigned date for controls

#Digital rectal exam or PSA test within 5 years before reference date

^<4% of men reported any male sexual partners

Table 2

Odds ratios and 95% confidence intervals of advanced prostate cancer by *T. vaginalis* antibody serostatus

	***T. vaginalis* status**			
	Seronegative		**Seropositive**	
Advanced prostate cancer*				
cases/controls (n)	122/139		24/42	
Model 1	1.00 (ref)	---	0.60 (0.34-1.06)	0.08
Model 2	1.00 (ref)	---	0.51 (0.28-0.93)	0.03
Fatal prostate cancer				
cases/controls (n)	89/139		20/42	
Model 1	1.00 (ref)	---	0.69 (0.38-1.27)	0.23
Model 2	1.00 (ref)	---	0.57 (0.30-1.08)	0.09
Caucasian men only**				
Advanced prostate cancer*				
cases/controls (n)	109/131		21/36	
Model 1	1.00 (ref)	---	0.65 (0.36-1.20)	0.17
Model 2	1.00 (ref)	---	0.60 (0.32-1.13)	0.11
Fatal prostate cancer				
cases/controls (n)	78/131		17/36	
Model 1	1.00 (ref)	---	0.75 (0.39-1.44)	0.39
Model 2	1.00 (ref)	---	0.68 (0.35-1.34)	0.27

Model 1: Adjusted for age and study

Model 2: Model 1 + race, prostate cancer screening history, and smoking status

*Advanced prostate cancer includes men with metastases and fatal prostate cancer

**Models not adjusted for race