THE JOURNAL OF
SEXUAL MEDICINE

ONCOLOGY

REVIEW

Sexual Activity and Risk of Prostate Cancer: A Dose–Response Meta-Analysis

Zhongyu Jian, MD, Donghui Ye, MD, Yuntian Chen, MD, Hong Li, MD, and Kunjie Wang, MD

ABSTRACT

Introduction: The role of sexual activity (SA) on prostate cancer (PCa) risk is still controversial.

Aim: To determine the associations among number of female sexual partners, age at first intercourse, ejaculation frequency (EF), and the risk of PCa.

Methods: A systematic literature search on MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was conducted to identify the relevant studies published before April 2018. We calculated the summary odds ratio (OR) and 95% CI to determine the association between SA and PCa risk. A 2-stage dose-response meta-analysis was performed to explore the trend from the correlated log OR estimates.

Main Outcome Measures: Outcome measures included characteristics of included studies, associations among number of female sexual partners, age at first intercourse, as well as EF and PCa risk.

Results: A total of 21 case-control studies and 1 cohort study with 55,490 participants (14,976 patients and 40,514 controls) were included in this meta-analysis. Linear and significant dose–response associations were found among number of female sexual partner as well as age at first intercourse and PCa risk, an increment of 10 female sexual partners associated with a 1.10-fold increase of PCa risk (OR 1.10, 95% CI 1.01–1.21), and the risk of PCa was decreased by 4% for every 5-year delay in age at first intercourse (OR 0.96, 95% CI 0.92–0.99). Although no linear association was observed between EF and the risk of PCa, moderate EF (2–4 times per week) was significantly associated with a lower risk of PCa (OR 0.91, 95% CI 0.87–0.96).

Clinical Implications: Modification of SA factors would appear to be a useful low-risk approach to decreasing the risk of PCa.

Strengths & Limitations: This is the first dose–response meta-analysis performed to describe the association between SA and PCa risk. However, the direction of causality between SA and risk of PCa should be interpreted with caution because most included studies used case-control design.

Conclusion: Meta-analysis of the included studies indicated that men with fewer sexual partner numbers, older age at first intercourse, and moderate frequent ejaculation were associated with a significantly decreased risk of PCa. **Z Jian Z, Ye D, Chen Y, et al. Sexual Activity and Risk of Prostate Cancer: A Dose-Response Meta-Analysis. J Sex Med 2018;XX:XXX–XXX.**

Key Words: Prostate Cancer; Sexual Activity; Sexual Partners; Ejaculation; Meta-Analysis

INTRODUCTION

Prostate cancer (PCa) is one of the most common cancers in the elderly population. In fact, PCa may be the most common non cutaneous cancer in men. It was estimated that 233,000 men were diagnosed with PCa, and 29,480 men died of this disease in 2014 in the United States.[1] There are some established disease risk factors, such as age, family history, and race, which are not modifiable.[2] Some modifiable risk factors, including diet and physical activities, may provide certain benefits for secondary prevention.[3] However, the role of other modifiable risk factors, especially sexual activity (SA), is still controversial.

In fact, there has been extended research focused on the association between SA and PCa. The main studied factors of SA are ejaculation frequency (EF), number of sexual partners, and

Received April 23, 2018. Accepted July 10, 2018.

Department of Urology, Institute of Urology (Laboratory of Reconstructive Urology), West China Hospital, Sichuan University, Chengdu, Sichuan, People's Republic of China.
The first 2 authors contributed equally.

https://doi.org/10.1016/j.jsxm.2018.07.004

age at first intercourse. The impact of sexually transmitted infections (STIs) and vasectomy on PCa risk are also reported by 2 updated meta-analysis.[4,5] SA is hypothesized to affect PCa pathogenesis through numerous mechanisms. On one hand, increased SA may be associated with higher androgenic activity, which may be an indicator of higher PCa risks,[6] although it is not concluded until now and was used to exam. On the other hand, SA means increasing the potential of exposure to STIs, which has been confirmed to be associated with a higher risk of PCa.[4] Moreover, there is another hypothesis called the prostate stagnation hypothesis. High frequency of ejaculation is thought to reduce the concentration of carcinogenic substances within prostatic fluid,[7] so reduced EF may be an etiologic risk factor for PCa.

A meta-analysis in 2002 concluded that the risk of PCa was associated with increasing EF and number of sexual partners, but the age at first intercourse was not associated with PCa risk.[8] However, more studies were published afterward, and different conclusions were made. Therefore, we conducted a systematic meta-analysis to draw a more precise estimation of their associations. Because categories of EF, number of sexual partners, and age at first intercourse differed between studies, which may complicate the interpretation of the pooled results, we also performed a dose—response analysis.

The role of SA on PCa risk is still controversial. The aim of the present study is to verify, using meta-analytic methods, whether age at first intercourse, number of female sexual partners, and EF represent possible risk factors for PCa, considering all available data from studies that meet the inclusion criteria.

METHODS

We performed this systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9]

Search Strategy

A systematic literature search on MEDLINE, Cochrane Central Register of Controlled Trials, and Web of Science, based on PRISMA guidelines, was conducted to identify relevant studies. The time frame spanned from the startup of these databases to April 2018. The search was restricted to the English language and human participants. The search strategy was developed using the Population, Exposure, Comparison, and Outcome Study (PECOS) framework. The search strategy used in MEDLINE was the Medical Subject Headings (MeSH) terms and text words, which were ((("Coitus"[MeSH] OR First intercourse OR Sexual Intercourse OR Coital Frequency)) OR ("Ejaculation"[MeSH] OR Ejaculation)) OR ("Sexual Partners"[MeSH] OR Multiple Partners OR Sexual Partners)) AND ("Prostatic Neoplasms"[MeSH] OR Prostate Cancer OR Prostatic Neoplasms). The literature search was performed by 2 independent reviewers. Disagreements were resolved by consensus or consultation with a third reviewer.

Eligible Criteria

Studies matching the eligible criteria listed below were included in further meta-analysis. The PECOS evidence base consisted of the following: (1) participants: men with PCa; (2) exposure: the exposure of EF, number of female sexual partners, or age at first intercourse; (3) comparisons: compared with the population-based or hospital-based population controls; (4) outcomes: diagnosis of PCa; and (5) study design: all study designs were accepted. In addition, the relative risk (RR) estimate (odds ratios [OR] or hazard ratio) with their 95% CIs could be extracted (or information to calculate them). Review, meta-analysis, meeting abstracts, comments, editorials, letters, congress reports, and case reports were not included in our study. For multiple publications based on the same study sample, only the most recently published results were included.

Data Extraction and Quality Assessment

The data were extracted by 2 authors independently. Disagreements were resolved by consensus or consultation with a third author. The following information was extracted from each eligible article: the name of first author, year of publication, original country, study period, study design, sample size, measurement of SA (EF, number of female partners, and age at first intercourse), the RR, and corresponding 95% CIs for each category of SA.

Newcastle—Ottawa Scale (NOS)[10] was used to evaluate the methodological quality of the included studies by 2 independent authors. Each study was assessed based on 3 broad perspectives: selection, comparability, and exposure with a total score of 9. A score more than 6 indicated that the study was of high quality. Disagreements were resolved through discussion and re-evaluation of the methodology of the study in question.

Statistical Analyses

All statistical analyses of this meta-analysis were performed with software (Stata, Version 14; Stata Corporation, College Station, TX, USA). Mean effect size (OR and 95% CI) was extracted from each study, and log OR was calculated by the inverse-variances method to obtain a RR and its 95% CI. For each study, the lowest dose represented the reference category and the highest dose represented the greatest dose category. Moderate EF group represented in-between EF category.

Heterogeneity of studies was assessed using the Q and I^2 statistics[11]; $I^2 > 50\%$ or $P < .1$ meant a significant heterogeneity. The fixed effect model was used to access data if the heterogeneity was not significant. Otherwise, the random effect model was applied. Subgroup analyses were conducted to explore the source of heterogeneity. Meta regression analysis[12] was conducted to explore the relation between the covariates (publication year, sample size, study population, NOS score, geographic area,