



Original article

Ejaculatory frequency and the risk of aggressive prostate cancer: Findings from a case-control study

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Abstract

Objectives: Recent literature reports inverse associations with ejaculator frequency and prostate cancer (PC). We sought to explore the relationship between ejaculatory frequency from ages 20 to 50 and subsequent development of aggressive PC.

Material and methods: We conducted a case-control study sampling 2,141 men from private urology practices in Victoria, Australia. Cases were defined as men with high grade or high stage PC and controls being biopsy negative men. Ejaculation frequency recalled at age decades 20, 30, and 40 second was assessed by questionnaire. Unconditional multivariable logistic regression models were used to generate odds ratios (ORs).

Results: An inverse association with ejaculatory frequency at age 30 to 39 was observed (OR per 5-unit increase per week = 0.83, 95% CI: 0.72–0.96) but not at ages 20 to 29 (OR = 1.01, 95% CI: 0.89–1.14) or ages 40 to 49 (OR = 0.95, 95% CI: 0.81–1.12). This result differed between men with new sexual partners after age 30 (OR = 0.77, $P = 0.009$) and those with no new partners (OR = 0.97, $P = 0.8$) though the test for a difference between these estimates was not significant ($P = 0.11$).

Conclusion: We found only weak evidence of an inverse association between ejaculatory frequency in the fourth decade of life and advanced PC, which was not significantly modified by number of new sexual partners. No relationship was found for ejaculatory frequency in the third and fifth decades of life. © 2017 Elsevier Inc. All rights reserved.

Keywords: Case-control; Ejaculation; Epidemiology; Prostate; Prostate cancer

1. Introduction

Prostate cancer (PC) has some established nonmodifiable risk factors such as family history and ethnicity but modifiable risk factors of similar strength are lacking [1]. This lack might be linked to the phenotypic heterogeneity of PC, which has been exaggerated in past decades by

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widespread prostate specific antigen (PSA) testing, which increased the diagnosis of prostatic tumors with low metastatic potential [2].

The function of the prostate is to add proteins and other molecules to the ejaculate. These exert an effect on semen liquefaction though the precise role this plays in reproduction is not defined [3]. It is plausible that greater frequency of ejaculation and thus repeated demands on the functional role of the prostate may alter the risk of subsequent PC. A recently published cohort study [4] reported an inverse association between increased ejaculation in the third and fifth decades of life and organ confined PC mirroring findings from our earlier case-control study [5]. Both studies used the same instrument to measure ejaculatory frequency, a questionnaire that we had developed to capture all ejaculations, not only those occurring during episodes of sexual intercourse. These findings may be due to a differential in sex hormone levels or the accumulation of intraluminal secretions in the prostate, both being correlated to PC incidence in different ways [6,7]. We present the outcomes from a case-control study aiming to assess the relationship with aggressive/advanced PC (APC). We assessed exposure by asking for a numerical estimate of ejaculatory frequency at different ages regardless of whether these occurred from intercourse or masturbation. This permitted a direct evaluation of the exposure effect rather than using surrogates such as age at first intercourse, number of partners or marital status, which have been described more commonly in the literature [8–12].

2. Material and methods

2.1. Study design

The design was a case-control study based on a sampling frame of urology practices in the State of Victoria, Australia, following identification through the Victorian Cancer Registry (VCR). To minimize information biases to which case-control designs are prone, controls were sought that had experienced similar levels of clinical investigation, in particular an elevated PSA test, but who proved to be biopsy negative for PC. Ethical approval was received from the Cancer Council Victoria ethics committee (#0910).

2.2. Case definition and recruitment

Eligible cases were patients with aggressive PC meeting the following four criteria: (A) histological Gleason grade 8 or higher from radical prostatectomy specimen or in the absence of surgical specimen, from transrectal biopsy or transurethral resection or pathological stage T3+ or N1 or M1 as defined by the AJCC sixth edition staging manual, (B) diagnosis between 1 January 2010 and 30 June 2014,

(C) age <77 at time of contact, and (D) able to complete questionnaires in English.

Cases were first identified by the VCR, which manages the statutorily mandated population cancer register for the state of Victoria, Australia. Following identification of a potential case, the VCR informed the treating urologist of their intent to approach the patient and confirmation that they met the inclusion criteria for the study. At this stage, the treating clinician could inform the VCR that they did not want the patient contacted. Following permission from the urologist, the patient was then approached for consent to participate in the study. Once this was obtained, the self-administered questionnaire was posted to the participant by the research team.

2.3. Control definition and recruitment

Controls were recruited from the same urology practices as the cases. Practices identified patients eligible according to the following criteria: (A) PC malignancy excluded by transrectal biopsy, (B) PSA <10 ng/ml but elevated for their age, (C) age <77 years, and (D) able to complete a questionnaire in English.

2.4. Questionnaire

The questionnaire is a 48-page document that asks about numerous lifestyle factors. It was mailed with a return envelope to the subjects following consent to participate in the study being received.

2.5. Sexual history definitions

The questions on sexual history captured the frequency of ejaculation during the participants' most sexually active year within 3 age decades, 20, 30, and 40 second. A single numerical estimate either per day, week or month was asked and recorded. These were standardized to a weekly value by multiplying the per day responses by 7 and dividing per month responses by 4. No distinction was made between ejaculation from sexual intercourse, masturbation or nocturnal emissions and respondents were asked to combine these in their estimate. By not asking for an "average frequency" we prevent participants making calculation errors, aiding in accurate recall and also avoid "normative" language, which itself introduces bias [13,14]. Additionally, a numerical estimate of the number of new sexual partners a participant had after age 30 years was asked. This was dichotomized to "none" and "any" new partners for analysis.

2.6. Covariate definitions

Age was defined in years at the date the questionnaire was completed for both cases and controls. Body mass index (BMI) was calculated from responses to questions on

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