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Association between lifetime alcohol consumption and prostate cancer risk: A case-control study in Montreal, Canada

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ABSTRACT

Background: Alcohol intake may increase the risk of prostate cancer (PCa). Many previous studies harbored important methodological limitations.
Methods: We conducted a population-based case-control study of PCa comprising 1933 cases and 1994 controls in Montreal, Canada. Lifetime alcohol consumption was elicited, by type of beverage, during in-person interviews. Odds ratios (OR) and 95% confidence intervals (CI) assessed the association between alcohol intake and PCa risk, adjusting for potential confounders and considering the subjects' PCa screening history.
Results: We observed a weak, non-significant positive association between high consumption of total alcohol over the lifetime and risk of high-grade PCa (OR = 1.18, 95% CI 0.81–1.73). Risk estimates were more pronounced among current drinkers (OR = 1.40, 95%CI 1.00–1.97), particularly after adjusting for the timing of last PCa screening (OR = 1.52, 95%CI 1.07–2.16). These associations were largely driven by beer consumption. The OR for high-grade PCa associated with high beer intake was 1.37 (95%CI 1.00–1.89); it was 1.49 (95%CI 0.99–2.23) among current drinkers and 1.68 (95% CI 1.10–2.57) after adjusting for screening recency. High cumulative consumption of spirits was associated with a lower risk of low-grade PCa (OR = 0.75, 95%CI 0.60–0.94) but the risk estimate no longer achieved statistical significance when restricting to current users. No association was found for wine consumption.
Conclusion: Findings add to the accumulating evidence that high alcohol consumption increases the risk of high-grade PCa. This association largely reflected beer intake in our population, and was strengthened when taking into account PCa screening history.

1. Introduction

High alcohol intake is a risk factor for many cancers, including those of the oral cavity, pharynx, larynx, esophagus, colorectum, liver and female breast [1]. In 2012, the International Agency for Research on Cancer concluded that there was little evidence in support of an association between consumption of alcoholic beverages and risk of prostate cancer (PCa) [1]. However, subsequent studies have suggested that alcohol intake might in fact increase risks for this cancer [2–8]. In a meta-analysis conducted recently, there was indication of a positive association between alcohol consumption and risk of overall PCa [9].

Earlier studies may have been more likely to harbor methodological limitations, resulting in a shift in findings over time. These include insufficient statistical power, crude alcohol exposure metrics, timing of assessment, non-differentiation of types of beverages, low exposure levels in some study populations, use of various disease endpoints, lack of consideration of cancer aggressiveness, confounding or biases [1,10]. Recent reports also stress the importance of considering PCa screening when studying associations with alcohol use [11–13]. Moreover, previous

Abbreviations: PCa, prostate cancer; PSA, prostate screening antigen; DRE, digital rectal exam; OR, odds ratio; CI, confidence interval.

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evidence rests largely on studies overlooking the issue of latent (undiagnosed) cancers in non-cases.

The objective of the present study was to provide additional evidence on the alcohol intake – PCa relationship while minimizing previous methodological issues.

2. Materials and methods

2.1. Study population

We used data from the Prostate Cancer & Environment Study (PROtEuS) [14], a large population-based case-control study in Montreal assessing the role of potential risk factors in PCa development.

Eligible subjects were men, younger than 76 years at diagnosis or selection, residents of Greater Montreal, registered on Quebec's permanent electoral list (continually updated) and Canadian citizen. Cases were all patients newly diagnosed with primary PCa, actively ascertained through pathology departments across the main French hospitals (7 out of 9 hospitals) in the Montreal area between 2005 and 2009. Based on registry information, this covered at least 80% of all PCa cases diagnosed in the area during the study period. Control subjects were selected concurrently from the population-based provincial electoral list of French-speaking men, and frequency-matched to cases by 5-year age groups.

The participation rate among eligible subjects was 79% for cases and 56% for controls. The study was approved by the Ethics Committees of all participating institutions. All participants provided written informed consent.

2.2. Data collection

Eligible subjects were sent an introductory package and were reached by telephone by interviewers to set up an appointment. In-person interviews collected socio-demographic and lifestyle characteristics, family history of cancer, medical and PCa screening histories, and self-reported weight and height. Subjects reported their overall physical activity level at work (Very/Moderately/Not very active), at home (Very/Moderately/Not very active) and their engagement in any leisure physical activity during adulthood [15], along with their frequency of use of 44 fruit and vegetables.

For subjects who reported ever consuming alcohol once a month for one year or more, lifetime alcohol consumption was recorded for beer, wine and spirits. Drinks were reported in commonly used servings, i.e., 375 ml for beer, 125 ml for wine and 45 ml for spirits. For each beverage type, each time the pattern of intake changed, participants were asked to report their drinking habits, including the time period (age started and age ended) and the frequency of drinking (number of drinks per month, week or day). This allowed taking into account changes in intake levels over the lifespan.

The degree of aggressiveness of PCa, defined by the Gleason score, was extracted from prostate biopsy pathology reports.

2.3. Exposure variables

Lifetime cumulative exposure variables were created for each type of beverages. These were defined as the product of the average number of drinks consumed per day and the duration of drinking in years for beer, wine, and spirits, and expressed as drink-years.

A composite exposure variable was also constructed to express the cumulative exposure to total alcohol by taking into account the ethanol content by volume of each type of beverages. Using the quantities of 14.8 g of ethanol per drink of beer, 11.8 g per drink of wine, and 14.2 g per drink of spirits [1,16], we calculated the cumulative intake in total grams of ethanol. The latter was divided by 14, which corresponds to the average amount of ethanol per drink weighted by the proportion of each type of drink in our study population, to estimate the total amount of alcohol used, in drink-years, standardized for ethanol content.

2.4. Statistical analyses

Odds ratios (OR) and 95% confidence intervals (CI) were used to assess the association between alcohol consumption and PCa risk. Risks of low-grade and high-grade (Gleason scores >7 or [4+3]) PCa were estimated using unconditional polytomous logistic regression. Two models were developed. Model 1 was adjusted for the age at diagnosis or interview (continuous), ancestry (Black/Asian/European/Other), first-degree family history of PCa (Yes/No), education (Elementary/High School/College/University), smoking (cigarette pack-years, continuous), overall physical activity (Very/Moderately/Not very active), maximum body mass index (BMI, continuous), frequency of use of fruit and vegetables (categorical), and self-reported history of diabetes (Yes/No). Analyses focusing on specific beverages were adjusted for other types of beverages. Model 2 included all variables in Model 1 as well as the timing of the last PCa screening by prostatic specific antigen (PSA) and/or digital rectal exam (DRE) (Within the last 2 years, 2–5 years earlier, More than 5 years earlier, Never screened, Don't know).

Alcohol exposure was analyzed using quartiles of total alcohol, beer and wine drink-years, and tertiles of spirit drink-years (because of fewer drinkers) based on the distribution among controls. Non-drinkers (subjects who reported having consumed alcohol less than once a month over a year, or less) or non-drinkers of the specific beverage under study constituted the reference category in analyses for total alcohol and for specific beverages, respectively.

Since men who stopped drinking or never drinkers may differ in some qualitative way from current alcohol consumers, analyses were also conducted among current drinkers, defined as subjects reporting drinking in the two years before diagnosis or interview. In this analysis, subjects in the lowest quartile/tertile category were considered as the reference.

Sensitivity analyses were also performed excluding proxy respondents (<4% of subjects), restricting the sample to subjects of European ancestry (86% of subjects), and restricting controls to men who had been screened (PSA and/or DRE) in the 2 years preceding the interview to reduce the likelihood of undiagnosed PCa among controls.

3. Results

3.1. Study population

The characteristics of study participants are presented in Table 1. Average age was about 64 years. The case series included a greater proportion of subjects of African ancestry but a lower proportion of Asian subjects than controls. Cases reported more often a first-degree family history of PCa than controls. A lower proportion of cases than controls had been diagnosed with diabetes. Cases had a slightly lower maximum BMI. About 99% of cases and 76% of controls had been exposed to PCa early detection efforts in the form of PSA and/or DRE testing within the 2 years preceding the interview. There were little differences in terms of education, smoking history, physical activity, and frequency of use of fruit and vegetables according to case/control status.

3.2. Alcohol consumption patterns

Cases and controls presented similar percentages of never, current and former users of total alcohol (Table 1). They also