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Short Communication

The impact of alcohol consumption on the risk of cancer among men: A 20-year follow-up study from Finland

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ABSTRACT

Introduction: Alcohol consumption is associated with certain cancer types and cancer deaths but there is paucity of information on the relationship between alcohol and total cancer risk. Hence, we examined this association.

Methods: We analysed data from a prospective population-based cohort study of 2627 men from Eastern Finland who had no history of cancer at baseline. There were 515 incident cancer cases accrued over 52,540 person years during the 20 years of follow-up.

Results: We observed a linear relationship between alcohol consumption and cancer. Men within the highest quintile of alcohol consumption (>115 g/week) had a 42% increased risk of total cancer compared with those within the lowest quintile (relative risk (RR) 1.42, 95% confidence interval (CI) 1.07–1.88; P_{trend} = 0.03) after adjusting for age, smoking, total energy intake and cardio-respiratory fitness. The results were the same after excluding cancer cases diagnosed during the first 2 years of follow-up. Men who consumed ⩾28.2 g/day of alcohol (median) had a relative risk of 1.22, 95% CI 1.03–1.46; P-value 0.03) compared to those who consumed less.

Conclusion: About 6.7% of the cancer cases in this cohort were due to alcohol consumption. Strategies to reduce cancer burden need to incorporate reduction in alcohol consumption, probably beyond the level currently recommended.

1. Introduction

The impact of cancer on global burden of diseases is increasing and is expected to increase further over time; from an estimated 10 million new cases in the year 2000 to an estimated 15 million new cases by the year 2020.[1,2] Likewise, the 6 million yearly deaths from cancer constitute about 12% of all worldwide deaths and this is expected to increase

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to about 10 million yearly deaths by the year 2020.[1,3] It has been estimated that about 3.6% of cancer cases worldwide are attributable to alcohol.[4]

While alcohol consumption is an established risk factor for certain types of cancer[5–7] its relationship with some other cancer types are still debatable.[5,6] Most studies exploring the association of alcohol with cancer have focused on its effects on specific cancer sites and on cancer mortality.[8–12] There is paucity of epidemiological studies on alcohol and total cancer even though cancer incidence, rather than cancer mortality is a more relevant measure to estimate the burden of cancer.[4] Studies conducted in Japan have observed increased risks of cancer associated with alcohol consumption.[13,14] The increased risks were observed for both alcohol-related cancers and non-alcohol-related cancers.[13] Likewise, a meta-analysis of several studies involving 18 cancer sites reported a dose–response increased risk for total cancer with increasing alcohol consumption.[5]

We analysed data from a cohort of randomly selected men from Finland who have been followed up for up to 20 years to determine the relationship between alcohol consumption and cancer risk among men.

2. Materials and methods

2.1. Study population

The men were participants in the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD). This is a prospective population-based study designed to investigate risk factors for cardiovascular diseases and other health related outcomes among middle-aged men from Eastern Finland. The study population consisted of a random age-stratified sample of 2682 men who were aged 42, 48, 54 or 60 years at the time of baseline examination between March 1984 and December 1989. In all, 3235 men were eligible to participate of which 193 were excluded because of underlying serious diseases and 83% (2682) volunteered to take part. Complete data on alcohol consumption were available for 2627 men. The study protocol was approved by the research ethics committee of the University of Kuopio. All men gave written informed consent.

2.2. Alcohol consumption

Alcohol consumption was assessed with a structured quantity and frequency method using the Nordic alcohol consumption inventory.[15,16] Usual frequency of intake and usual dose (in glasses or bottles) were recorded for each type of drinks (beer, wine, strong wine, spirits) with a structured response form, which assessed both total alcohol intake and the timing or pattern of drinking (usual number of drinks per session). The measures of average weekly intake of all alcoholic beverages were calculated on the basis of known alcohol content of each type of drinks and reported doses and frequencies of drinking sessions. A third of a litre bottle of ordinary beer (class iii in Finland) contains 12 g of ethanol, strong beer (class iv) contains 14 g of ethanol which is the ethanol equivalent of 1 portion of hard liquor. Serum gamma-glutamyl transpeptidase (GGT) and Mean Corpuscular Volume (MCV) were determined from baseline blood samples as biomarkers of excessive alcohol use.

2.3. Outcome events

All cancer cases diagnosed in Finland since 1953 have been reported to the Finnish Cancer Registry (FCR). Coverage of the national cancer registry is virtually complete with no loss to follow-up.[17] Our study cohort was record linked to the FCR by using the Finnish personal identification code which is given to all residents in Finland. All cancer cases that occurred between the study entry (March 1984–December 1989) and 31th December 2008 were included. There were 515 cancer cases during a follow-up period of 20 years corresponding to 52,540 person years. Prostate cancer constituted the most incident type of cancer (175) followed by lung cancer (73), colorectal cancer (66) and genito-urinary tract cancers (50).

2.4. Other variables

A subject was described as a smoker if he had ever smoked on a regular basis and had smoked cigarettes, cigars or pipe within the past 30 days. The number of cigarettes, cigars and pipefuls of tobacco currently smoked daily and the duration of regular smoking in years were recorded on a self-administered questionnaire that was checked by an interviewer. The lifelong exposure to smoking was estimated as the product of the number of smoking years and the number of tobacco products smoked daily until the time of baseline examination. Detailed descriptions of measurements of other variables, especially cardio-respiratory fitness and energy intake have been given elsewhere.[18]

3. Statistical analysis

Descriptive data are presented as median (10th and 90th percentiles). Subjects were grouped into five quintiles. The weekly alcohol consumption within the quintiles were (i) 1st quintile; men who consume < 1.3 g of alcohol, (ii) 2nd quintile; 1.3–17.2 g/week, (iii) 3rd quintile; 17.3–48.8 g/week (iv) 4th quintile; 48.9–115.3 g/week and (v) 5th quintile > 115.3 g/week. We considered a priori, potential confounders such as age, examination year, family history of cancer, cigarette smoking, four categories (non-smoker, 110/day, 11–20/day and $\geqslant$21/day), cardio-respiratory fitness, socio-economic status, body mass index (BMI) in categories (<25, 25–29,= 30 kg/m^2), vegetable consumption and total energy intake. Cox proportional hazards model was used to examine the relationship between alcohol consumption and cancer risk. Likelihood ratio test was applied to assess the statistical significance of the variables, and possible interactions between them. The final model included age, smoking, cardio-respiratory fitness and energy intake because the other variables did not change the risk estimates by up to 10%.

In secondary analyses, we excluded cancer cases diagnosed within the first two years of follow-up. We also collapsed the cohort into 3 groups (i) abstainers (ii) quintiles 2–4 and a few men in quintile 1 who were technically not abstainers but consume very little alcohol (<1.3 g/week) and

(iii) quintile 5. The risk estimates were very similar to those obtained using the five categories and are thus not presented. The population-attributable fraction (PAF) is the percentage of a disease in a population that is due to a specific exposure.[19] We calculated the PAF of alcohol on total cancer risk using the formula: PAF = pd [(RR – 1)/RR], where pd is the proportion of cases exposed to a given exposure category of alcohol and RR is the adjusted relative risk for this category.[20] The 95% confidence interval for the PAF was estimated using the formula proposed by Greenland; 1 – (1 – AF) exp (±1.96 $VL^{1/2}$).[20] Statistical analyses were done using SPSS package [version 16 for windows (SPSS, Inc., Chicago, IL)].

4. Results

The median age was the same for all 5 quintiles (54.3 years). Men within the lowest quintile of alcohol consumption had the lowest median physical activity, and vegetable consumption but the highest total energy intake and consumption of fruits and berries. Men within the highest quintile of alcohol consumption had the lowest median fruits and berries consumption but the highest median BMI (27.1), and blood glucose (4.7 mmol/L). There was a correlation between alcohol consumption and biomarkers for alcohol consumption; S-GGT (*rs*; 0.35, *P*-value = 0.001) and MCV (*rs*; 0.30, *P*-value = 0.001) (Table 1).

The incidence rate for cancer among men within the 5th quintile of alcohol consumption was 141/10,000 compared to 97/10,000 among those within the 1st quintile. In the multivariate adjusted model, the relative risk for developing cancer among men who consumed the highest amount of alcohol was 1.42 (95% confidence interval (CI) 1.07–1.88; P_{trend} = 0.03) compared to those with the least consumption. Excluding cancer cases diagnosed during the first two years of follow-up did not make a difference to the results as the relative risk comparing men within the 5th quintile to those within the 1st quintile was practically the same (RR 1.42, 95% CI 1.07–1.89; P_{trend} 0.04). Almost 7% (6.7%; 95% CI 3–13) of the cancer cases in this cohort during the 20-year follow-up period was due to high alcohol consumption (Table 2). Men who consumed more than 28.2 g/day of alcohol (median level) had a slightly elevated risk (RR 1.22, 95% CI 1.03–1.46; *P*-value 0.03) compared to those who consumed less after adjusting for confounders (table not shown).

Table 1 – Baseline characteristics of study population expressed as median (10th and 90th percentiles).

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Age (years)	54.3(48.3, 60.5)	54.3(42.9, 60.4)	54.3(42.8, 60.4)	54.3(42.7, 60.1)	54.3(42.5, 60.3)
Smokers (%)	14.5	26.2	32.2	38.7	50.1
Physical activity (kcal/day)	69.9(0.1, 316.9)	91.2(6.1, 332.6)	87.9(8.7, 363.2)	94.7(10.6, 330.4)	78.4(1.8, 332.9)
BMI (kg/m^2)	26.5(22.6, 31)	26.1(22.7, 30.8)	26.2(22.6, 31.1)	26.5(22.9, 31.3)	27.1(23.1, 33.2)
Socio-economic status	14(7, 19)	13(5, 19)	12(4, 19)	12(4, 19)	13(5, 19)
Vegetable consumption over 4 days (g)	267.3(136.6, 444.5)	282.2(148.9, 447.5)	275.3(138, 430.9)	286.7(154, 444.8)	268.8(138, 442.1)
Fruits and berries consumption over 4 days (g)	150(25.9, 373.3)	132.4(19.6, 343)	132.6(4.4, 338.2)	137.8(1.2, 357)	121.3(0, 310.7)
Energy intake over 4 days (kJ)	9905(6990, 13,649)	9837(7129, 13,380)	9554(6692, 12,932)	9613(6632, 12,686)	9751(6761, 13,166)
Blood glucose (mmol/l)	4.6(4, 5.4)	4.6(4, 5.4)	4.5(4, 5.3)	4.6(4, 5.3)	4.7(4.1, 5.8)
Alcohol consumption, weekly (g)	0(0, 1.4)	8.8(3.9, 15.4)	32(18.7, 45.5)	76(53, 105)	198(127.7, 450.8)
Gamma-glutamyl transaminase (U/l)	16(10, 34)	18(10, 44)	20(12, 47)	22(12, 51)	33(15, 88)
Mean Corpuscular Volume (fl)	90.2(84.7, 95.5)	90.7(85.1, 96.2)	91.7(86.4, 97.7)	92.4(86.2, 98.6)	94.1(88.3, 100.4)

Table 2 – RRs (95%CI) of all-cause cancer according to quintiles of alcohol consumption among Finnish men followed up for up to 20 years.

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P_{trend}
All						
Number of subjects (cases)	525(90)	526(102)	526(104)	525(101)	525(118)	
Incidence rate/10,000	97	107	115	109	141	
Relative risk (95% CI)	1.0(reference)	1.07(0.80–1.41)	1.18(0.89–1.57)	1.08(0.81–1.43)	1.42(1.07–1.88)	0.03
Excluding cases diagnosed during the first 2 years of follow-up						
Number of subjects (cases)	525(88)	526(101)	526(96)	525(94)	525(115)	
Relative risk (95% CI)	1.0(reference)	1.08(0.81–1.44)	1.11(0.83–1.49)	1.03(0.76–1.32)	1.42(1.07–1.89)	0.04

Adjusted for age, cigarette smoking, cardio-respiratory fitness, energy intake and family history of cancer.

5. Discussion

In this population-based cohort study with a long follow-up period and low alcohol consumption, we confirmed a positive relationship between alcohol consumption and cancer.

The results from our study are notable given the fact that only colorectal cancer is classified as an alcohol associated cancer among the most incident cancers in our cohort. Prostate and lung cancer cases make up almost half of the cancer cases in this cohort but evidence linking alcohol consumption to their aetiology are still inconclusive.[21,22] Despite this, we still observed a 42% increased risk of cancer related to alcohol consumption in the cohort. The results from our study are similar to those from previous studies which noticed increased risks of total cancer among men with the highest alcohol consumption within a population.[5,13,14] The observed excess risk among men within the highest group of alcohol consumption in our cohort was similar to the excess risks, ranging from 40% to 61%, observed in the Japanese studies.[13,14] However, the quantities of alcohol consumed by the at-risk groups in the various studies differ. The consumption level associated with increased risks in our cohort was lower than that observed in other studies. While we cannot proffer a reason for this relatively lower intake being associated with increased risks, it may have important public health implications. This is because the European code against cancer[23] recommends keeping daily alcohol consumption between 20 and 30 g daily whereas in our cohort, men who consumed $\geqslant$28.2 g/day of alcohol (median level) had increased risk of cancer compared to those who consumed less.

The fraction of cancer cases attributable to alcohol consumption in this cohort is higher than the 3.6% worldwide estimate derived by Boffetta and colleagues at the International Agency for Cancer Research (IARC).[4] It is however very similar to the population-attributable fraction obtained for Europe A in the same study, to which Finland belongs to. The implication for cancer control within populations is that reducing alcohol consumption can lead to a reduction in cancer burden. However, it has been shown that alcohol consumption has increased in Finland since the 1960s.[24] In this cohort, even though the overall probability of drinking did not change during an 11-year follow-up period, there was an increase in the average weekly consumption and in the probability of heavy drinking among the cohort of 42-year-olds.[25]

Alcohol can induce carcinogenesis in the different organs either through local or systemic effects. Previously, alcohol was believed to be a co-carcinogen, rather than a carcinogen and that the carcinogenic effects are mainly due to its main metabolite, acetaldehyde,[26] but recently both alcohol and acetaldehyde have been classified as being carcinogenic to humans.[27] Apart from acetaldehyde production, alcohol can also promote carcinogenesis by inducing cytochrome P450 2E1, inducing global DNA hypomethylation by depleting S-adenosylmethionine, causing accumulation of Iron with its associated oxidative stress and impairing retinoic acid production.[26,28] Other mechanisms include alcohol's effects in reducing immunosurveillance, acting as a solvent for other carcinogens, and causing nutritional deficiencies.[27]

Strengths of our study include its prospective population-based nature. Response rate was high, follow-up was long and complete because of the unique personal identifier in the Finnish population. Assessment of alcohol consumption took place at baseline before cancer cases was diagnosed thereby minimising recall bias. We had information on a range of other lifestyle factors which we controlled for thereby minimising confounding. Our study also had the following limitations. Alcohol consumption was assessed based on a questionnaire, thus subject to underreporting or any other misclassification. There is however no reason to believe that any reporting bias is likely to be systematically differential across drinking groups. The questionnaire had previously been validated using biochemical markers of excessive alcohol use such as MCV and GGT, but nevertheless, we cannot completely rule out misclassification. Our study cohort included only men thus we cannot generalise the results to women. Also, it should be noted that we investigated the association of alcohol consumption with total cancer risk and not specific cancer sites (especially with regard to alcohol-related and non-alcohol-related cancers), since there are few site-specific cases, as the effects of alcohol on different cancer sites will differ.

In conclusion, alcohol consumption is associated with an increased risk of cancer among men. Strategies to reduce cancer burden need to incorporate reduction in alcohol consumption, probably beyond the level currently recommended.

Conflict of interest statement

None declared.

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