Cancer Causes and Control **15**: 571–580, 2004.
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Alcohol drinking may increase risk of breast cancer in men: a European population-based case–control study

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Received 12 November 2003; accepted in revised from 3 March 2004

Key words: alcohol drinking, breast neoplasms, case–control studies, male, risk factors.

Abstract

Objective: It has been estimated that alcohol drinking increases the risk of breast cancer in women by approximately 7% for each increment of 10 g alcohol per day. However, the few studies conducted on breast cancer among men have failed to detect an association with quantitative measures of alcohol drinking, even if the alcohol intake is generally higher in men than in women. On the other hand, increased risks of male breast cancer were inconsistently reported in alcoholics or patients with liver cirrhosis. We have investigated the role of alcohol drinking in male breast cancer using data collected in a population-based case–control study on seven rare cancers, conducted in Denmark, France, Germany, Italy, and Sweden.

Methods: The cases were 74 histologically verified male breast cancer patients aged 35–70 years. The controls (n = 1432) were selected from population registers, and frequency-matched to the cases by age group and geographic area. To check for consistency, a separate analysis was conducted using as controls the patients with a rare cancer other than male breast recruited simultaneously in the European study (n = 519 men).

Results: Based on population controls, the risk of developing breast cancer in men increased by 16% (95% CI: 7–26%) per 10 g alcohol /day ($p < 0.001$). An odds ratio of 5.89 (95% CI: 2.21-15.69) was observed for alcohol intake greater than 90 g per day, as compared with light consumers (< 15 g per day). Similar associations were observed when other rare cancers patients were used as controls.

Conclusion: We found that the relative risk of breast cancer in men is comparable to that in women for alcohol intakes below 60 g per day. It continues to increase at high consumption levels not usually studied in women.

Introduction

The relationship between alcohol ingestion and risk of breast cancer has been investigated in many epidemiological studies among women. Most studies have reported positive associations, but increased risks have not been found consistently, presumably because of the modest true relative risks associated with the levels of alcohol intake generally observed among the women included in these studies. Recently, an analysis has been conducted on alcohol and tobacco data collected in 53 epidemiological cohort and case–control studies on

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breast cancer risk among women, representing over 80% of the relevant information worldwide. On the whole, it was demonstrated that the risk of breast cancer is increased by 7.1% for each increment of 10 g alcohol per day (approximately 1 drink per day) [1].

The evidence that alcohol ingestion increases the risk of breast cancer in women has not been supported by similar findings on breast cancer in men [2–7]. Male breast cancer is rare, *i.e.* approximately 100 times less frequent than female breast cancer, and it has not been studied frequently. Only a few etiological factors have been suggested, including gynaecomastia, previous testicular pathology, Klinefelter's syndrome [8], or mutations on the BRCA2 gene [9]. It has been suggested that alcohol increases the risk of breast cancer through an elevation of serum levels of sex hormones produced by the adrenal glands, a mechanism that has been observed in a controlled trial among postmenopausal women [10]. Although this mechanism could operate in men as well, previous case–control studies using quantitative measures of alcohol drinking, such as mean daily consumption, did not report an association with male breast cancer. In other studies examining the association between male breast cancer and indicators of heavy drinking, such as chronic alcoholism or liver cirrhosis of alcoholic origin, the results have been mixed. Incidence of male breast cancer was not increased in a study among men with a hospital discharge diagnosis of alcoholism [11]. Other studies have reported an association between male breast cancer and chronic alcoholism [12, 13] that was statistically significant in a meta-analysis [8], or with liver cirrhosis [14, 15], suggesting that male breast cancer risk may be increased among the heaviest drinkers.

To investigate further the effect of alcohol drinking on breast cancer risk among men, we have used the data collected in a European population-based case-control study on [7] rare cancers, which was initially carried out with a main focus on occupational risk factors. Male breast cancer risk could be investigated in men with elevated alcohol intake, because the study was conducted in countries ranking among those with the highest alcohol consumption per adult. According to the World Health Organization, the consumption of pure alcohol in 1990, estimated by dividing the total alcohol production and trade by the adult population aged 15 years or older, was 16.2 l (about 35 g/day) in France, 14.0 l (30 g/day) in Germany, 11.5 l in Italy and Denmark (25 g/day), whereas it was only 9.2 liters (20 g/day) in the USA [16]. Thus, the present study of male breast cancer among European men could help to clarify the association between alcohol and breast cancer previously observed in women, and may contribute to a better understanding of the purported mechanisms of alcohol carcinogenesis.

Methods

A European population-based case-control study was conducted simultaneously for seven sites of rare cancer, including male breast, using the same group of population controls. The study was carried out in five countries (Denmark: the whole country subdivided in 10 areas; France: Calvados, Côte d'Or, Doubs, Hérault, Isère, Manche, Bas-Rhin, Haut-Rhin, Somme, Tarn; Germany: Hamburg, Bremen, Essen, Saarland, Saarbrücken; Italy: Turin, Florence, Padua; and Sweden: Umeå, Örebro/Uppsala, Linköping, Lund). These areas covered a population of 24 million persons in total. Other European countries participating to the same study, but using a hospital-based design with controls selected among colon cancer patients, were not included in the present analysis (Latvia, Portugal and Spain), because alcohol drinking is a suspected risk factor for colon cancer [17].

The cases were all men residing in the study areas, diagnosed with a cancer of the breast between 1 January, 1995 and 30 June, 1997, except in Sweden where the recruitment period started on 1 September, 1995 and in Denmark, where it ended on 31 December, 1996. Only cases aged 35–70 years at the date of diagnosis were included in the study. This age range was based on the assumption that occupational factors, one of the primary focus of the study, were not likely to be the cause of the disease in younger patients, and that their exposures would be too difficult to assess retrospectively with sufficient precision in older persons. Case ascertainment was based on regular contacts with pathology and clinical departments of the participating regions, and was ensured by frequent searches in patient registers. For each case, the original pathology report and, if possible, a histological slide representative of the tumor, were requested for review by a reference pathologist. In total, 85 male breast cancer cases were eligible for the study. The diagnosis of breast cancer was confirmed by reviewing a histological slide for 76 cases (89%), and the sole original pathology report for nine cases (11%).

Population controls were selected to serve as a common pool of controls for each of the seven groups of rare cancer cases included in the European study (as well as for a group of testis cancer patients recruited in Germany for another study). Controls were recruited concurrently with the cases, and selected at random from population registers in Denmark, Germany, Italy

Table 1. Number of men eligible for the study and number of participants, by country and case-control status. European study on rare cancers: countries with population-based design

Country	Cases of male breast cancer			Population controls		
	N eligible	N participants	(% of eligible)	N eligible	N participants	(% of eligible)[1]
Denmark	12	8	(67)	363	190	(52)
France	30	29	(97)	410	321	(78)
Germany	13	10	(77)	1042	573	(55)
Italy	20	20	(100)	284	208	(73)
Sweden	10	7	(70)	245	140	(57)
All	85	74	(87)	2344	1432	(61)

[1] Eleven interviewed controls were not included among participants because data on alcohol consumption was missing.

and Sweden and from electoral rolls in France. Controls were frequency-matched to the cases by year of birth (5-year strata), sex, and geographic area, in order to achieve a 4:1 ratio with the most frequent site of cancer in each stratum. As expected, this procedure yielded more than four controls per breast cancer case, but all controls were kept in the analysis in order to achieve maximum statistical power. All eligible subjects were invited to participate in an interview. Table 1 presents the number of participants by country and case-control status. Among male breast cancer patients, 74 cases (87%) completed the interview and were included in the analysis. Among population controls, the participation rate was high in France (78%) and Italy (73%), but it was lower ($< 60\%$) in Denmark, Germany, and Sweden, leaving 1432 (61%) population controls available for the analysis.

Differential participation rates between cases and population controls may bias study results if a subject's participation in the study is related to alcohol drinking. To see whether this problem actually occurred, we conducted a separate analysis using as controls all men with a rare cancer other than male breast recruited simultaneously in the European study. These rare cancer patients had a high participation rate, similar to that of male breast cancer cases. Among the 654 eligible men with another rare cancer, 519 (80%) completed the interview. They included cancer of the gallbladder and biliary tract (170 men), cancer of the small intestine (100 men), bone cancer (48 men), eye melanoma (111 men), thymoma (44 men), and mycosis fungoides (46 men).

After informed consent was obtained, a trained interviewer administered a structured questionnaire to participants during a face-to-face (France, Germany, Italy) or a telephone (Denmark, Sweden) interview. The questionnaire was first established in English and subsequently translated in the national language of participating countries. A back-translation in English was made to ensure uniformity. It included items on socio-demographic characteristics, previous medical conditions, lifestyle factors, anthropometric characteristics and a detailed occupational history. A previous disease or medical condition was considered as a potential risk factor for male breast cancer if it was diagnosed at least five years before the date of cancer diagnosis for the cases or before the date of interview for the controls. Information was also collected on tobacco smoking history. Alcohol intake was assessed in the questionnaire as the average number of drinks that the subject used to consume daily five years before the interview. It was calculated separately for each type of alcoholic beverage (wine, beer, aperitifs and liquor). Total alcohol intake was estimated using the same conversion factors as a previous European multicentric study [18]: 1 glass of beer (50 cl) = 20 g alcohol; 1 glass of wine (10 cl) = 9.4 g alcohol; 1 glass of aperitif (5 cl) = 7.25 g alcohol; 1 glass of liquor (5 cl) = 15.85 g alcohol. In the analysis by type of alcoholic beverage, aperitifs and liquors were grouped in the same category.

Because the lifetime history of alcohol intake was not recorded, some study subjects who declared that they consumed no alcohol five years ago may in fact be abstainers with previous problems of alcoholism. It has been shown that using nondrinkers as a reference group in alcohol-related studies is unsuitable [19], because the group of 'nondrinkers' may actually include ex-drinkers, leading to underestimating the true odds ratio. To minimize a possible bias, all analyses were first conducted using a reference category composed of both 'nondrinkers' and light drinkers (up to 15 g alcohol/day). All analyses were also conducted with abstainers excluded from the dataset, *i.e.*, using a reference group composed of light drinkers only, but the results changed only slightly, and are not shown here.

Odds ratios were calculated from unconditional logistic regression models using the STATA software [20]. Total alcohol intake was included in the models as

Table 2. Age distribution and mean alcohol consumption among participants. European study on rare cancers

Age distribution of respondents	Male breast cancer cases		Population controls		
	N	(%)	N	(%)	
<40	3	(4.1)	208	(14.5)	
40–44	3	(4.1)	171	(11.9)	
45–49	9	(12.2)	147	(10.3)	
50–54	12	(16.2)	153	(10.7)	
55–59	12	(16.2)	196	(13.7)	
60–64	15	(20.3)	239	(16.7)	
65+	20	(27.0)	318	(22.2)	
All	74	(100.0)	1432	(100.0)	$p = 0.04$
Alcohol consumption (g Alcohol/Day)	Mean	(s.e.)[1]	Mean	(s.e.)	p[2]
Denmark	32.1	(6.4)	34.2	(1.7)	0.80
France	46.4	(6.3)	33.3	(1.4)	0.01
Germany	41.4	(9.7)	26.9	(1.0)	0.05
Italy	46.9	(7.2)	38.3	(1.9)	0.20
Sweden	30.2	(6.5)	19.8	(1.3)	0.09
All	42.8	(3.5)	30.3	(0.6)	< 0.0001

[1] standard error of the mean
[2] t-test: comparison of means between cases and controls.

a categorical variable using predefined cutoff points of 15, 30, 45, 60, 75 and 90 g alcohol/day. In the analyses by type of alcohol, grouping these categories was necessary to avoid too small numbers. To estimate the increase in risk per 10 g alcohol/day, a continuous variable for alcohol intake was used in separate models. Adjustment for age (continuous) and recruitment area was performed in all models, since these variables were used as stratification variables to select the controls. To control for confounding, we also adjusted for several variables associated with risk in the univariate analyses. These variables included body mass index (continuous) and some previous medical conditions (present or absent). Adjustment for tobacco smoking (current smoker, ex-smoker, never smoker) was also conducted, because tobacco smoking is usually correlated with alcohol intake, and because it has been associated, albeit inconsistently, with the risk of female breast cancer [21].

Results

The age distribution in Table 2 shows that more population controls than male breast cancer cases are under the age of 45 years. This is explained by the frequency matching of controls by age to all the rare cancer sites included in the European study, and by an older age at diagnosis for male breast cancer than for the other cancers. Table 2 also shows that the mean alcohol consumption is significantly higher in cases than in controls. Among controls, the mean alcohol consumption ranges from 19.8 in Sweden to 38.3 g alcohol/day in Italy.

Table 3 presents odds ratios for male breast cancer associated with alcohol drinking. A sharp increase in risk with increasing alcohol intake is observed, and the odds ratios reach statistical significance for consumption levels above 60 g alcohol/day. An almost six-fold increase in risk is observed in the highest alcohol exposure category (> 90 g alcohol/day), as compared with light and non-drinkers. The risk increases by 16% for each increment of 10 g alcohol/day ($p < 0.001$). Table 3 also presents odds ratios for other risk factors associated with male breast cancer, and for tobacco smoking. Gynecomastia, diabetes, fertility problems of male origin, and head injury, as well as body mass index were significantly associated with risk in the univariate analyses. Other suspected risk factors, including testicular pathology and liver cirrhosis, were not associated with risk in our data. None of the male breast cancer patients and only five controls reported liver cirrhosis, resulting in an odds ratio of zero that cannot be interpreted due to low statistical power. The association between alcohol drinking and male breast cancer changed only slightly after adjustment for previous medical conditions (gynecomastia, diabetes, fertility

Table 3. Odds ratios associated with total alcohol intake and other selected factors in male breast cancer

	Cases	Controls	OR univariate[a]	95% CI	OR multivariate[b]	95% CI
Total alcohol (g/day)						
0–15[c]	13	381	1.00	Ref.	1.00	Ref.
>15–30	19	556	1.11	0.51–2.37	0.87	0.30–2.47
>30–45	11	238	1.23	0.53–2.86	1.37	0.46–4.08
>45–60	10	122	1.98	0.81–4.86	2.28	0.73–7.11
>60–75	6	50	4.53	1.52–13.53	4.45	1.12–17.66
>75–90	6	36	5.28	1.70–16.42	4.68	1.07–20.55
>90	9	49	5.89	2.21-15.69	5.62	1.54–20.52
Alcohol (per 10 g/day)			1.16	1.07–1.26	1.17	1.05–1.30
Smoking status						
Never smoker	26	386	1.00	ref.	1.00	Ref.
Current smoker	25	522	0.81	0.44–1.48	1.03	0.45–2.37
Ex smoker	23	529	0.68	0.38–1.23	0.71	0.31–1.64
Gynecomastia						
No	59	1398	1.00	Ref.	1.00	Ref.
Yes	7	10	21.70	6.67–70.57	23.42	4.65–117.97
Diabetes						
No	67	1370	1.00	Ref.	1.00	Ref.
Yes	7	52	2.99	1.21–7.40	1.92	0.42–8.73
Fertility problems						
No	49	1066	1.00	Ref.	1.00	Ref.
Yes	3	23	6.03	1.44–25.21	4.87	0.78–30.40
Head injury						
Never	60	1231	1.00	Ref.	1.00	Ref.
Ever	13	182	2.36	1.20–4.63	2.91	1.17–7.22
Body mass index (maximum) per 1 kg/m^2			1.09	1.02–1.15	1.08	0.99–1.17

[a] Adjusted for age and geographic area only.
[b] Adjusted for age, geographic area, and all other variables listed in the table.
[c] Reference category includes nondrinkers (5 cases and 104 controls) and light drinkers <15 g/day alcohol.

problems, head injury), body mass index, and tobacco smoking. Adjustment did not change substantially the odds ratio per 10 g alcohol/day, indicating no overall confounding. Odds ratios associated with previous medical conditions also remained elevated, but had wider confidence intervals.

As can be seen in Table 4, when rare cancer patients other than male breast available in the European study were used as controls, the odds ratios were slightly lower than those in Table 3, using population controls. However, a sharp increase in the risk associated with alcohol drinking was still apparent, with a five-fold increased risk in men drinking more than 90 g alcohol/day. Overall, a 14% increase in risk for each increment of 10 g alcohol/day was observed, close to the 16% increase estimated using population controls. Adjustment for confounders yielded similar results.

The odds ratios associated with an increment of 10 g alcohol/day, calculated with population controls, are tabulated by country in Table 5. Male breast cancer risk increases by 15 – 27%, depending on the country, except in Denmark where a slightly decreased risk is observed. However, the likelihood ratio test comparing models with and without an interaction term between country and alcohol was not significant (chi statistics 1.90, 4 df, $p = 0.75$), indicating no statistically significant heterogeneity between countries. Adjustment for previous medical conditions listed in table 3, body mass index, and tobacco smoking changed the results only slightly, but generally led to higher odds ratios (Table 5).

Table 4. Odds ratios associated with total alcohol intake using the group of rare cancer patients other than male breast as controls

	Cases	Controls	OR univariate[a]	95% CI	OR multivariate[b]	95% CI
Total alcohol (g/day)						
0–15[c]	13	116	1.00	Ref.	1.00	Ref.
>15–30	19	210	0.91	0.41–2.01	0.67	0.22–2.04
>30–45	11	59	1.56	0.62–3.93	1.82	0.52–6.44
>45–60	10	61	1.62	0.63–4.23	1.41	0.41–4.90
>60–75	6	27	2.25	0.73–6.93	3.90	0.78–19.53
>75–90	6	24	2.42	0.75–7.87	2.74	0.53–14.06
>90	9	22	5.05	1.63–15.65	4.66	1.02–21.30
Alcohol (per 10 g/day)			1.14	1.04–1.26	1.17	1.03–1.33

[a] Adjusted for age and geographic area only.
[b] Adjusted for age, geographic area, tobacco smoking, gynecomastia, diabetes, head injury, fertility problems and body mass index.
[c] Reference category includes nondrinkers (5 cases and 45 controls) and light drinkers < 15 g/day alcohol.

Table 5. Odds ratios per 10 g alcohol/day by country

	N cases	N controls	OR univariate[a]	95% CI	OR multivariate[b]	95% CI
Denmark	8	190	0.94	0.65–1.35	1.13	0.63–2.03
France	29	321	1.15	1.02–1.29	1.34	1.10–1.61
Germany	10	573	1.23	1.01–1.49	1.12	0.73–1.72
Italy	20	208	1.20	1.00–1.44	1.29	1.02–1.63
Sweden	7	140	1.27	0.94–1.71	1.27	0.76–2.12
All countries	74	1432	1.16	1.07–1.26	1.17	1.05–1.31

[a] Adjusted for age and geographic area.
[b] Adjusted for age, geographic area, tobacco smoking, gynecomastia, diabetes, head injury, fertility problems and body mass index.

The odds ratios associated with each type of alcoholic beverage are shown in Table 6. When types of alcoholic beverage were studied separately in different models (OR_1), increased risks and a significant dose–response gradient were observed for wine and for beer, but not for aperitifs and liquors. There was no case of male breast cancer above 60 g alcohol/day for beer and for aperitifs and liquor, so that odds ratios could not be calculated in these groups. Because the different types of alcohol may be correlated with each other, we also fitted a model where all types of alcoholic beverages were included at the same time (OR_2). Odds ratios for wine and beer did not decrease substantially, suggesting an independent effect on breast cancer risk. The decrease was more pronounced for aperitifs and liquor, indicating that some confounding from wine and beer may exist. Further adjustments for previous medical conditions and body mass index did not affect the results and are not shown. Overall, this analysis does not indicate a clear differential effect of the type of alcoholic beverage on the risk of male breast cancer.

Discussion

This is the first study reporting an association between alcohol drinking and male breast cancer.

Selection bias

One possible limitation of our study is a lower participation among eligible population controls than among eligible cases. This could have resulted in an overestimation of the odds ratios if, among controls, heavy drinkers had been less likely to participate in a study than moderate drinkers. However, no evidence of such a selection bias exists in our data. Several population surveys conducted in Europe have indicated that respondents and nonrespondents do not differ

Table 6. Odds ratios by type of alcoholic beverage

	Cases	Controls	OR_1[a]	95% CI	OR_2[b]	95% CI
Wine (g alcohol/day)	50	1260	1.00	Ref.	1.00	Ref.
0–30	14	129	1.92	0.93–3.98	1.81	0.87–3.77
30–60	10	43	5.36	2.19–13.11	5.22	2.07–13.12
>60						
			1.27	1.10–1.46	1.25	1.08–1.44
Wine (per 10 g alcohol/day)						
Beer (g alcohol /day)	58	1194	1.00	Ref.	1.00	Ref.
0–15	10	181	1.61	0.76–3.40	1.50	0.69–3.24
15–30	6	39	5.42	1.88–15.61	2.86	1.73–15.31
30–60	0	18	–	–	–	–
>60						
Beer (per 10 g alcohol/day)			1.17	1.00–1.37	1.13	0.96–1.33
Aperitifs/liquor (g alc/day)	65	1324	1.00	Ref.	1.00	Ref.
0–15	8	84	1.95	0.85–4.48	1.43	0.59–3.48
15–30	1	17	0.92	0.11–7.66	0.65	0.07–5.88
30–60	0	7	–	–	–	–
>60						
Aperitifs/liquor (per 10 g alcohol/day)			1.15	0.91–1.44	1.04	0.81–1.34

[a] Adjusted for age and geographic area only.
[b] Adjusted for age, geographic area, and for the other two types of alcoholic beverage.

according to alcohol consumption [22, 23], with one study reporting prevalence of unsafe alcohol consumption even higher among respondents than among non respondents [24]. In addition, the mean alcohol consumption by country among our population controls (Table 2) was close to what could be expected on the basis of national data on alcohol intake per adult, as estimated by the World Health Organization [16]. Furthermore, we have observed a regular gradient of male breast cancer risk with alcohol intake, which was confirmed in countries with high participation rates such as France and Italy, and which is hardly compatible with the presence of a selection bias. More importantly, we had the opportunity to assess the effect of a potential selection bias among our population controls. This was done by replacing the group of population controls by a group of patients with rare cancers other than male breast and recruited simultaneously in the European study. Differential participation according to alcohol consumption cannot be suspected *a priori* among these patients, because the participation rate was high (80–90% of eligible cases were interviewed, depending on the cancer site) and similar to that of male breast cancer cases. A comparison of the male breast cancer cases with these other rare cancer controls (n = 519 men) yielded an odds ratio of 1.14 (95% CI : 1.04–1.26) for each increase of 10 g alcohol/day, a value close to the odds ratio of 1.16 estimated using the original group of population controls. Alcohol drinking was found to be a weak risk factor for some of the other rare cancer sites included (*e.g.* small intestine) [25]. Therefore, we also performed an analysis using the eye melanoma cases only as controls (n = 111 men, over 90% respondents among eligible cases), since alcohol is not a suspected etiological agent for this cancer (results not shown). The odds ratio per 10 g alcohol/day was 1.36 (95% CI : 1.15–1.61). These findings reinforce the idea of a real link between alcohol drinking and male breast cancer.

Confounding from other risk factors

Besides alcohol, our data permitted to investigate a number of factors previously suspected of increasing male breast cancer risk [8]. We found associations with

gynaecomastia [2, 26], diabetes [26, 27], head injury 13, problems of male fertility [26], and high body mass index [27]. Adjusting for these potential confounders, and for tobacco smoking, which generally correlates with alcohol drinking, did not change the association between alcohol and male breast cancer. The strong association with gynecomastia is difficult to interpret because of a possible recall bias, as the cases may be more inclined to report this problem, which is common during puberty or adolescence. The risk associated with head injury remained significantly elevated after adjustment for alcohol drinking and other factors, and might increase breast cancer risk through an alteration of prolactine levels, as suggested by other authors [13]. These factors may deserve further attention in future analyses. Other factors such as mumps orchitis [2], cryptorchidism [3, 26], and liver cirrhosis [2, 12–14] are suspected of increasing the risk of male breast cancer, but this could not be confirmed in the present data.

Comparison with other male breast cancer data

Studies based on quantitative measures of alcohol consumption

Previous case–control studies conducted in the USA [2–5], Canada [6], and Greece [7] have investigated the role of alcohol drinking in male breast cancer. None of them has reported a clearly increased risk of male breast cancer in relation to alcohol consumption. In two early case–control studies carried out in the USA [2,3], the average weekly alcohol intake did not differ significantly between cases and controls, although in one study [3], the cases reported a somewhat greater consumption of beer and wine than the controls. In another US study where cases and controls were identified from death certificates [4], alcohol drinking was ascertained from a next-of-kin of the deceased person. No increased risk was observed among men who ingested more than five drinks per day, but it was acknowledged by the authors that the odds ratio could be biased toward unity, because drinking was overrepresented in dead controls. Two recent population-based case–control studies were conducted in the USA and Canada. In the US study [5], subjects were classified according to the total number of drinks in life, but no data on daily or weekly alcohol consumption are presented, so that the same criteria as in our study could not be used to identify heavy drinkers. In the Canadian study [6], the highest category for alcohol drinking was 10 servings or more per week, a moderate alcohol consumption. Finally, in a hospital-based case-control study carried out in Greece [7] based on 23 cases, male breast cancer risk was not elevated for occasional (<7 drinks per week) or for regular (≥ 7 drinks per week) drinkers, compared with nondrinkers. No further categorization of alcohol drinking was made.

The use of different indices of alcohol intake makes a comparison between male breast cancer studies difficult. Although the increased risk of male breast cancer in relation to alcohol consumption seems to be at odds with previous investigations, our findings may be explained by the possibility to identify groups of heavy drinkers in European populations. This is supported by reports on mean alcohol intake per adult based on sales and production of alcohol [16], which is higher in Western European countries, particularly Denmark, France, Germany and Italy, than in North America, where most studies on male breast cancer and alcohol have been conducted.

Studies among men with problems of alcoholism and with liver cirrhosis

Chronic alcoholism was not assessed in the present study, but it was associated with male breast cancer risk in previous case–control investigations [12, 13], leading to an OR = 1.9 (95% CI : 1.1–3.2) in a meta-analysis [8]. Conversely, in a recent cohort study exploring male breast cancer risk in over 145,000 men with a hospital discharge diagnosis of alcoholism conducted in Sweden [11], male breast cancer incidence was not increased in the cohort as compared with the general Swedish population (standardized incidence ratio = 1.1 based on 13 observed cases). Although this study does not support an effect of alcohol drinking in male breast cancer, it should be noted that it included men with chronic alcoholism as well as men with acute alcoholic intoxication, possibly on only one occasion. Thus, the mean quantity of alcohol ingested daily, which was not known from the data, might not be elevated for all cohort members.

A few studies have also reported male breast cancer risk in men with liver cirrhosis. An association between alcohol-induced liver cirrhosis and male breast cancer should be observed, if alcohol drinking is a cause of breast cancer. Unfortunately, this association could not be assessed from the present data, since no male breast cancer case and only five controls reported having the disease, leading to insufficient statistical power. This number of liver cirrhosis in our data is compatible with the prevalence of cirrhosis among heavy drinkers, which is usually below 10% (see, for example [28]). However, an association between male breast cancer and liver cirrhosis was reported in a previous case-control study [OR = 2.7] [14], although it was not statistically significant. In a cohort study of over 11,000 men with liver

cirrhosis conducted in Denmark, a statistically non significant increased risk of male breast cancer (standardized incidence ratio = 4.0) was also reported [15]. Two out of the three observed male breast cancer cases occurred in men with alcoholic cirrhosis.

Although the evidence of an increased male breast cancer risk in alcoholics or liver cirrhosis patients is weak and inconsistent, there is some indication in previous investigations of an elevated risk of male breast cancer in these groups. Studies in groups of heavy drinkers may be helpful to explore these associations more thoroughly.

Comparison with female breast cancer data

The average alcohol consumption among control men in the present study was 30.3 g alcohol/day (Table 2), compared with 6.0 g/day only among the control women from developed countries included in the collaborative reanalysis of female breast cancer studies [1]. Among men in the present study, 18% reported consumptions of at least 45 g alcohol/day, whereas among women, this percentage was only 1% [1]. Thus, this study on male breast cancer allowed the estimation of breast cancer risks for high levels of alcohol intake, not usually observed among women.

We found that the odds ratio for breast cancer in men is similar to that in women for levels of alcohol intake below 60 g per day (5–6 drinks per day). In the range 0–60 g alcohol/day, i.e., the range observed in women, the increase of male breast cancer risk per 10 g alcohol/day was 5.5%, close to the value of 7.1% observed for female breast cancer [1]. Above 60 g alcohol/day, a level of alcohol intake not frequently observed among women, our data show a steep rise in male breast cancer risk, with an increase in risk as high as six-fold in men who reported consumption greater than 90 g alcohol/day (> 9 drinks per day). It would be important to know if these risks of breast cancer observed for male heavy drinkers also apply to female heavy drinkers. Although some studies do not support the hypothesis of a substantially increased breast cancer risk in heavy drinkers among women [29], further studies of breast cancer focusing on heavy female drinkers are necessary.

Conclusion

In this multicenter population-based case–control study in Europe, we have observed a clear increased risk and a dose-response gradient of male breast cancer with alcohol intake. Breast cancer risk in men is similar to that in women for alcohol consumption below 60 g/day, but it increases sharply at higher levels of alcohol intake, levels not frequently explored in studies on female breast cancer due to the small number of heavy drinkers among women. This first report of an association between alcohol drinking and male breast cancer still needs to be confirmed in other studies conducted in populations where high levels of alcohol intake can be identified.

Acknowledgements

The authors wish to thank Denis Hémon for his thoughtful comments on the manuscript.

The study 'Occupational risk factors for rare cancers of unknown etiology' was supported by the European Commission, DGXII, BIOMED programme (grant no. BMH1 CT 93-1630). Support was also provided in Denmark by the Danish Epidemiology Science Centre, the Danish National Research Foundation, the Strategic Environment Programme; in France by the 'Ligue Nationale contre le Cancer', 'Fondation de France', 'Institut National de la Santé et de la Recherche Médicale' (INSERM), 'Association pour la Recherche contre le Cancer' (ARC), Ministère de l'Environment; in Germany by the Federal Ministry for Education, Science, Research and Technology (BMBF), grant no. 01-HP-684/8; in Italy by MURST, Ministry of Labour, Italian Association for Cancer Research, Compania San Paolo/FIRMS; in Sweden by the Örebro County Council Research Committee, Swedish Council for Work Life Research, Research Foundation of the Department of Oncology in Umeå, Swedish Society of Medicine, Lund University Hospital Research Foundation, Gunnar, Arvid and Elsebeth Nilsson Cancer Foundation.

Appendix

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