



Original Paper

Alcohol and Breast Cancer in the Swiss Canton of Vaud

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The relationship between alcoholic beverage drinking and the risk of breast cancer was considered using data from a case-control study of breast cancer conducted between 1990 and 1995 in the Swiss Canton of Vaud on 230 incident cases of breast cancer below age 75 years, linked with the Vaud Cancer Registry, and 507 controls admitted to the same network of hospitals for a wide spectrum of acute, non-neoplastic, non-hormone-related conditions. Overall, 70.4% of cases versus 57.4% of controls consumed alcohol, corresponding to a multivariate odds ratio (OR) of 1.5 (95% confidence interval (CI): 1.1–2.2). The ORs were 1.3 for < 1 drink per day, 1.8 for 1 to 2, 1.5 for 2 to 4, and 2.7 for > 4 drinks per day, and the trend in risk with dose was significant. The association was consistent for wine (OR = 2.0), beer (OR = 2.6) and spirits (OR = 2.0), and was apparently stronger in premenopausal women, whereas no noticeable interaction was observed with any of the hormonal or reproductive risk factors for breast cancer. The alcohol-related risk was unrelated to duration; the OR was 1.8 for women who started drinking below the age of 30 years and 1.4 for those starting at the age of ≥ 30 years. Thus, the present study confirms that alcohol is a correlate of breast cancer risk in this European population, where alcohol drinking among women is common and relatively high. Assuming that this association reflects causality, in terms of attributable risk, alcohol could explain 25% (8–42%) of breast cancer cases. Copyright © 1996 Elsevier Science Ltd

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INTRODUCTION

THERE ARE several epidemiological studies indicating that alcohol consumption is related to breast cancer risk in women. Most data, however, come from North America or Northern Europe, where alcohol drinking among women is relatively infrequent and generally moderate [1, 2]. Thus, even in the report from the large American Nurses' Health Study, the highest consumption category was > 1 drink per day [3].

Data from Europe, and particularly from Southern Europe, are of specific interest, since they are able to provide information on higher consumption levels. Thus, studies conducted in Northern Italy [4–8], France [9] and

Spain [10] give relative risks between 1.5 and 2.5 for levels of intake of 20 or 30 g of ethanol, i.e. 2 to 3 drinks per day. However, further information on these higher levels of alcohol intake is required to improve understanding the pattern of dose-risk relationship, and hence for any inference on a possible causal role. It is also of interest to analyse further the possible role of various types of alcohol beverages, and their potential impact on breast cancer rates, on a population scale.

To achieve these major objectives, we analysed data from a case-control study conducted in French-speaking Switzerland, a region where alcohol consumption by women is not only frequent, but also consistently higher than in Northern Europe and America, and where breast cancer incidence rates are among the highest in Europe [11]. The study was specifically designed to address the issue of dietary factors (including alcohol) on breast carcinogenesis [12, 13].

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MATERIALS AND METHODS

Since January 1990, a case-control study of breast cancer has been conducted in the Swiss Canton of Vaud within the framework of a larger co-operative study originally co-ordinated by the World Health Organization (WHO) SEARCH Programme of the International Agency for Research on Cancer [12]. The general design of this study has already been described [13]. This report is based on data collected before August 1995.

Cases were women with incident (i.e. diagnosed within the year before the interview), histologically confirmed breast cancer, who had been admitted to the University Hospital of Lausanne, Switzerland. Cases identified and interviewed were linked with the incidence data from the Vaud Cancer Registry [14], to verify comparability of baseline characteristics with incidence cases in the reference population of the Canton. A total of 230 cases, aged 27–75 years (median age 55 years), were interviewed.

Controls were women aged ≤ 75 years residing in the same geographical area, whose primary diagnosis was

judged to be unrelated to any of the known or suspected risk factors for breast cancer. Women were not included if they had been admitted for breast, gynaecological, hormonal, metabolic or neoplastic diseases. Controls were not singularly matched with cases, but were of similar catchment area and selected in comparable strata of age. A total of 507 controls aged 24–75 years (median age 57 years) were interviewed. They were admitted to the same University hospital in Lausanne for a wide spectrum of acute conditions, including traumas (29%, mostly sprains and fractures), non-traumatic orthopaedic diseases (11%, mostly low back pain and disk disorders), surgical conditions (35%, mostly abdominal, such as acute appendicitis or strangulated hernia), and miscellaneous other disorders (25%, including acute medical, eye, nose and throat, and other miscellaneous).

All interviews were conducted in the hospital. Less than 15% of subjects approached for interview (cases and controls) refused. The structured questionnaire included information on personal characteristics and habits (e.g. smoking,

Table 1. Distribution of 230 cases of breast cancer and 507 controls according to age and selected covariates (Vaud, Switzerland, 1990–1995)

Variable	Cases		Controls	
	<i>n</i>	%	<i>n</i>	%
Age (years)				
< 45	41	17.8	103	20.3
45–54	66	28.7	119	23.5
55–64	61	26.5	135	26.6
65–75	62	27.0	150	29.6
Education (years)				
< 11	135	58.7	318	62.7
≥ 11	95	41.3	189	37.3
Body mass index (kg/m ²)				
< 25	139	60.4	297	58.6
≥ 25	91	39.6	210	41.4
Number of births				
0	50	21.7	111	21.9
1–2	140	60.9	285	56.2
≥ 3	40	17.4	111	21.9
Age at first birth (years)				
< 25	83	36.1	203	40.0
≥ 25	97	42.2	192	37.9
Missing	50	21.7	112	22.1
Menopausal status				
Pre/In-menopause	78	33.9	172	33.9
Post	152	66.1	335	66.1
Age at menopause (years)				
< 50	83	36.1	177	34.9
≥ 50	69	30.0	157	31.0
Missing	78	34.3	173	34.1
Cigarette smoking				
Never	119	51.7	309	60.9
Ex	34	14.8	49	9.7
Current	77	33.5	149	29.4
Oral contraceptive use				
Never	139	60.4	354	69.8
Ever	91	39.6	153	30.2
Hormone replacement therapy				
Never	166	72.2	394	77.7
Ever	64	27.8	113	22.3
Family history of breast cancer				
No	208	90.4	491	96.8
Yes	22	9.6	16	3.2

physical exercise, a food frequency section), body mass index before diagnosis, a problem-oriented medical history, menstrual and reproductive factors, and history of lifetime use of oral contraceptives, menopause replacement therapy, and female hormone preparations for other indications. Information on alcohol consumption included, for each type of alcoholic beverage (wine, beer, other spirits), data on days per week and drinks per day, the age at starting and the duration of the habit, in years.

Odds ratios (ORs) of breast cancer, and the corresponding 95% confidence intervals (CI) of breast cancer according to various measures of alcohol drinking were derived from multiple logistic regression equations [15]. Two models were fitted, one including age only, and one including terms for age, marital status, education, age at menarche, parity, age at first birth, menopausal status, age at menopause, type of menopause, family history of breast cancer, smoking habits and oral contraceptives and hormone replacement therapy use. Since the results were similar, only the latter is presented.

RESULTS

Table 1 gives the distribution of cases and controls with reference to age and major covariates of interest. No appreciable difference was observed in relation to education, body mass index and cigarette smoking. Cases were less frequently multiparous, reported later age at first birth, slightly more frequent use of oral contraceptives and hormone replacement treatment and significantly, more frequently had a family history of breast cancer ($P < 0.01$).

The distribution of breast cancer cases and controls according to measures of alcoholic beverage consumption is given in Table 2. Overall, 70.4% of cases and 57.4% of controls consumed alcoholic drinks, corresponding to a multivariate OR of 1.5 (95% CI: 1.1–2.2). With reference to alcohol consumption, the ORs were 1.3 for < 1 drink

per day, 1.8 for 1 to < 2, 1.5 for 2 to 4, and 2.7 for > 4 drinks per day. The estimate for the highest consumption level, and the trend in risk with dose were significant. The ORs were consistently above unity for wine (OR = 2.0 for \geq drinks per day), beer (OR = 2.6 for beer drinkers versus non-drinkers), and spirits (OR = 2.0 for \geq 1 drink per day).

The relationship between alcohol consumption and breast cancer risk is further considered in Table 3 across separate strata of age and selected covariates. The association was somewhat stronger for regular drinkers at younger age (OR = 2.3) and in premenopausal women (OR = 5.4), with a significant interaction with menopausal status, and in women with higher body mass (OR = 2.6), earlier menopause (OR = 1.7) and first birth (OR = 2.3), whereas no appreciable or meaningful modifying effect was observed with reference to education, parity, oral contraceptive and hormone replacement treatment use, and an increasing risk with increasing drinks per day was observed across various strata of covariates examined.

Table 4 considers various time factors of alcohol drinking: there was no relationship with duration, the OR being 1.6 for < 20 years, 1.4 for 20 to 29 years, and 1.5 for \geq 30 years. With reference to age at starting alcohol consumption, the OR was 1.8 for women starting below age 30, and 1.4 for those starting at age 30 years or over. However, the confidence intervals of these two estimates overlap.

DISCUSSION

The present study confirms that alcohol drinking is a correlate of breast cancer risk [1–10] in this European population, and indicates that the risk is increased approximately 2–3-fold for the highest consumption levels of daily alcohol (> 4 drinks per day), and for each type of alcoholic beverage. Thus, the data are consistent not only with the overall

Table 2. Distribution of 230 breast cancer cases and 507 controls, odds ratios (ORs) and 95% confidence intervals (CIs) according to various measures of alcohol consumption (Vaud, Switzerland, 1990–1995)

	Cases		Controls		OR†(95% CI)	χ^2_1 (trend)
	<i>n</i> *	%	<i>n</i> *	%		
Teetotallers	68	29.6	216	42.6	1‡	
Consumers of alcoholic beverages	162	70.4	291	57.4	1.5(1.1–2.2)	
Total, alcoholic beverages (drinks/day)						
<1	65	28.3	149	29.4	1.3(0.8–1.9)	
1–<2	49	21.3	77	15.2	1.8(1.1–2.9)	
2–4	30	13.0	49	9.7	1.5(0.8–2.7)	
>4	18	7.8	15	3.0	2.7(1.3–5.8)	8.5§
Wine (drinks/day)						
>0–<1	69	30.0	154	30.4	1.2(0.8–1.9)	
1–<2	43	18.7	75	14.8	1.7(1.0–2.7)	
\geq 2	44	19.1	53	10.5	2.0(1.2–3.2)	9.6§
Beer (drinks/day)						
\geq 0.5	32	13.9	34	6.7	2.6(1.4–4.6)	
Spirits (drinks/day)						
>0–<1	49	21.3	66	13.0	1.8(1.1–2.9)	
\geq 1	12	5.2	15	3.0	2.0(0.9–4.7)	2.0

*For some variables, the sum of strata does not add up to the total because of missing values. †Estimates from unconditional multiple logistic regression models including terms for age, plus marital status, education, parity, age at first birth, menopausal status, age at menopause, family history of breast cancer, smoking habits, oral contraceptives and hormonal replacement therapy use. ‡Reference category. § $P < 0.01$.

Table 3. Odds ratios* (ORs) and corresponding 95% confidence intervals (CIs) of breast cancer in relation to average daily total alcoholic beverage consumption in separate strata of age and selected covariates (Vaud, Switzerland, 1990–1995)

Variable	OR (95% CI) of total alcoholic beverage consumption, drinks per day			(Number of cases)†	χ^2 (trend)
	0	<1	≥1		
Age (years)					
<50	1	2.0(0.9–4.4)	2.3(1.0–5.3)	(70)	3.9‡
50–59	1	1.5(0.7–3.4)	1.6(0.7–3.5)	(76)	1.3
60–75	1	0.9(0.4–1.8)	2.1(1.1–4.0)	(84)	5.4‡
Education (years)					
<11	1	1.4(0.8–2.4)	2.1(1.2–3.6)	(135)	7.6§
≥11	1	1.2(0.6–2.3)	1.4(0.7–2.7)	(95)	1.0
Body mass index (kg/m ²)					
<25	1	0.8(0.5–1.4)	1.5(0.9–2.5)	(139)	2.0
≥25	1	2.1(1.1–4.1)	2.6(1.3–5.0)	(91)	8.2§
Number of births					
0	1	0.8(0.3–2.2)	3.3(1.3–8.4)	(50)	6.6‡
1–2	1	1.5(0.9–2.5)	1.4(0.8–2.4)	(140)	1.8
≥3	1	1.2(0.5–3.2)	2.1(0.8–5.6)	(40)	2.0
Age at first birth (years)					
<25	1	1.5(0.8–3.0)	2.3(1.2–4.4)	(83)	6.8§
≥25	1	1.5(0.8–2.8)	1.1(0.6–2.1)	(97)	0.1
Menopausal status					
Pre/In-menopause	1	2.2(1.0–4.6)	5.4(2.5–11.9)	(78)	17.6§
Postmenopause	1	1.0(0.6–1.7)	1.3(0.8–2.2)	(152)	1.3
Age at menopause (years)					
<50	1	1.8(0.9–3.7)	1.7(0.8–3.5)	(83)	1.9
≥50	1	0.5(0.2–1.1)	1.1(0.5–2.1)	(69)	0.01
Oral contraceptive use					
No	1	1.2(0.7–2.0)	1.7(1.1–2.8)	(139)	4.7‡
Yes	1	1.6(0.8–3.5)	2.1(0.9–4.5)	(91)	3.4
Hormone replacement therapy					
No	1	1.2(0.8–2.0)	2.0(1.2–3.2)	(166)	8.1§
Yes	1	1.4(0.6–3.4)	1.4(0.6–3.3)	(64)	0.5
Family history of breast cancer					
No	1	1.3(0.8–2.0)	1.9(1.3–2.9)	(208)	9.8§
Yes	1	1.0(0.1–6.5)	0.8(0.1–6.5)	(22)	0.3

*Estimates from unconditional multiple logistic regression models, including term for the other variables shown in the table. †For some variables, the sum of strata does not add up to the total because of missing values. ‡ $P < 0.05$. § $P < 0.01$. ||Reference category. n.e., not estimable.

accumulated evidence on the relationship of alcohol to breast cancer, but also with the few data available for Southern Europe [4–10, 16], and support the indication, given by the updated European Code Against Cancer [17], of moderating alcohol drinking, particularly in women. Further, the data indicate that the association is independent of the type of alcohol beverage, suggesting that ethanol *per se* is a correlate of risk. No appreciable interaction or modifying effect emerged with any of the reproductive or hormonal risk factors for breast cancer [3, 5, 18, 19], although the relationship was somewhat stronger in premenopausal women. This was observed in some [3, 20, 21], but not other studies [5, 10, 22–24].

As in most epidemiological work [1–10, 16, 18–23], the ORs were practically unchanged after allowing for potential confounding factors, including cigarette smoking and other major correlates of alcohol drinking, or a number of known determinants of breast cancer. This study, moreover, was consistent with the suggestion that drinking at a young age is specifically related to the risk of breast cancer [25]

although the interactions with age at diagnosis or age at starting drinking were not significant. Still, the underlying biological model and the issue of causality remains open to discussion, mainly in the absence of a clear biological mechanism which may explain the association [2]. Although a detailed discussion of any such mechanism is beyond the scope of this work, possible interactions between alcohol intake and hepatic metabolism of carcinogens, steroid hormones and their serum levels and availability have been suggested [2, 26–28], but not consistently reproduced in animal or human studies [29, 30]. Inference on causation is also hampered by the lack of consistent duration–risk relationship [31].

With reference to potential limitations of the present study, although case recruitment was matched with a cancer registry [14], this is a hospital-based case-control study, and has therefore all the related strengths and weaknesses [15]. Of relevance in this study, however, are the satisfactory participation of cases and controls approached for interview, and the similar interview setting which should increase re-

Table 4. Odds ratios* (ORs) and 95% confidence intervals (CIs) of breast cancer in relation to duration of alcohol consumption and age at starting alcohol use. (Vaud, Switzerland, 1990–1995)

	Breast cancer	Controls	OR (95% CI)
Non-drinkers	68	216	1†
Duration of alcohol consumption (years)			
<20	47	90	1.6 (1.0–2.6)
20–29	47	82	1.4 (0.9–2.3)
≥30	68	116	1.5 (1.0–2.4)
Unknown	–	3	
Age at starting drinking (years)			
<30	70	111	1.8 (1.2–2.8)
≥30	92	178	1.4 (0.9–2.0)

*Estimates from unconditional multiple logistic regression models, including term for age, marital status, education, parity, age at first birth, age at menopause, family history of breast cancer, smoking habits, oral contraceptives and hormonal replacement therapy use. †Reference category.

liability and comparability of alcohol use [32]. Almost one-third of controls had traumatic conditions, which may be related to alcohol drinking, and hence lead to underestimating the real association. However, the ORs were similar when a separate comparison was made with major diagnostic categories of controls.

In terms of population attributable risk [33, 34], alcohol consumption explained 25% (95% CI: 8–42%) of breast cancer cases. Assuming that the ORs are unbiased, that the cases are representative of all breast cancer cases in this population [33], and the association reflects causality [16, 31, 35], this should make alcohol one of the major avoidable causes of breast cancer in this population.

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