

Fats in Seasoning and Breast Cancer Risk: an Italian Case-Control Study

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The relationship between consumption of fat in seasoning and risk of breast cancer was considered in a case-control study conducted in Northern Italy of 2663 cases of breast cancer and 2344 controls admitted in the same network of hospitals with acute, non-neoplastic and non-gynaecological conditions. Subjective scores corresponding to three levels (low, intermediate and high) of intake of butter, margarine and oil, together with a combined variable of these three items ("total fat"), were used to evaluate the personal use of fat in seasoning. Compared to low use, a slight but significant increase in risk was observed for intermediate and high intake of butter, oil and total fat with relative risks of 1.5 (95% confidence interval [CI], 1.1–1.9) for high intake of butter, 1.3 (95% CI, 1.0–1.6) for high intake of oil and 1.4 (95% CI, 1.2–1.7) for high intake of total seasoning fat. These results were not materially modified after allowance for a number of identified potentially distorting factors. The results of this study suggest that there is a positive association, although moderate, between breast cancer risk and intake of fat added in seasoning, which may represent an indirect indicator of the subject's attitude towards fat.

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INTRODUCTION

MOST OF the initial evidence linking breast cancer risk to diet comes from animal experiments [1] and from ecological studies on diet and breast cancer rates in different populations. On an international scale, strong positive correlations have been observed with measures of fat intake [2], calories, proteins, and selected food items such as milk, eggs, or meat [2, 3]. Similar correlations have been observed on national scale as well [4, 5]. Within Italy, for instance, breast cancer rates in various regions have been positively correlated with milk, cheese and meat consumption, and the correlations persisted after allowance for parity [5].

Unfortunately, the evidence from analytical epidemiology to date is not so clear. Case-control studies have reported associations with total energy, fats, proteins and specific food items such as fried foods, dairy products, beef and other red meat, pork and desserts [6–12]. The associations observed, however, were moderate and inconsistent. Some case-control studies found a direct association with fat, such as those from Canada, Israel and Holland [7, 12, 13]; in an Italian study the relative risk for the upper quartile of saturated fat reached 3.0 [14]. In other studies the association was weak and inconsistent [6, 15, 16] although the point estimates were above 1, whereas studies from the USA, Greece and Japan showed no evidence of positive association [9, 10, 17]. To further complicate the issue, three prospective studies from the USA [18–20] found no evidence of

any positive association with total fat intake, as well as with various types of fats.

To explain the positive associations observed in some Mediterranean populations, a greater variability of diet and a large range of fat intake have been advocated, although this topic is still open to debate [21]. In this article, therefore, we have re-examined the issue, using information available on taste for fat in seasoning from a large case-control study conducted in Northern Italy, whose general methodology and results in relation to various dietary factors have previously been described relative to the first 3 years of data collection [11].

SUBJECTS AND METHODS

Since January 1983 we have been conducting a case-control study of breast cancer in Northern Italy. Trained interviewers identified and questioned women admitted for breast cancer and for a wide spectrum of acute, non-neoplastic, non-gynaecological conditions to a network of University and general hospitals in the Greater Milan area. Overall participation rate was over 97% for both cases and controls.

The standard questionnaire included information on sociodemographic characteristics and habits; medical history; obstetrical data; history of lifetime use of contraceptive methods and use of other female hormones. Within a simplified dietary section, including frequency of intake of a few selected indicator foods, subjective scores (low, intermediate, high) were used to obtain information on fat intake in seasonings (butter, margarine and oil).

The present report is based on information collected before November 1989.

Cases

The cases were women with histologically confirmed breast cancer, diagnosed within the year preceding the interview, who had been admitted to the National Cancer Institute, to several University clinics or to the Ospedale Maggiore, including the

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Table 1. Distribution of 2663 cases and 2344 controls according to age, years of education, age at first birth, menarche and menopause. Milan, Italy, 1983–1989

	Cases		Controls	
	No.	%	No.	%
Age				
< 40	291	10.9	352	15.0
40–49	757	28.4	535	22.8
50–59	760	28.5	673	28.7
60–69	607	22.8	557	23.8
70–74	248	9.3	227	9.7
Education (years)*				
< 7	1391	52.2	1411	60.2
7–11	743	27.9	564	24.1
≥ 12	526	19.8	365	15.6
Age at first birth*				
Nulliparous	493	18.5	475	20.3
< 20	87	3.3	172	7.3
20–24	791	29.7	743	31.7
25–29	830	31.2	644	27.5
≥ 30	462	17.3	304	13.0
Age at menarche*				
< 12	485	18.2	430	18.3
12–14	1792	67.3	1493	63.7
≥ 15	379	14.2	419	17.9
Age at menopause				
Premenopausal	1122	42.1	884	37.7
< 40	94	3.5	112	4.8
40–44	197	7.4	222	9.5
45–49	424	15.9	456	19.5
50–53	636	23.9	511	6.8
≥ 54	190	7.11	159	

* The sum of strata does not add up to the total because of some missing values.

four major general hospitals in the Greater Milan area. A total of 2663 cases (aged from 23 to 74 years, median 53) was interviewed.

Controls

The comparison group comprised patients admitted for acute conditions to the same network of hospitals where cases had been identified. They had diseases other than malignant, hormonal or gynaecological diagnosed in the year before the interview. Of these, 35% were admitted for trauma, 27% for non-traumatic orthopaedic disorders, 13% for acute surgical conditions and 25% for other illnesses such as ear, nose, throat and dental disorders. A total of 2344 controls (aged 25–74, median 54) were interviewed.

Data analysis

We computed the relative risks (RR) of breast cancer, together with their 95% approximate confidence intervals (CI) [22], according to various levels of fat consumption. The index of total fat intake was simply derived by combining the scores (low = 1, intermediate = 2, high = 3) of self-reported intake of the three major types of dietary fat (butter, margarine and oil).

In the computation of relative risks, decade of age was

Table 2. No. (%) of cases and controls according to self-reported scores of consumption of various fats in seasonings*

Type of fat	Score					
	Low		Intermediate		High	
	Cases	Controls	Cases	Controls	Cases	Controls
Butter	1601 (60.1)	1524 (65.0)	909 (34.1)	717 (30.6)	153 (5.7)	103 (4.4)
Margarine	2219 (83.3)	1970 (84.0)	422 (15.8)	356 (15.2)	22 (0.8)	17 (0.7)
Oil	309 (11.6)	317 (13.5)	2008 (75.4)	1758 (75.0)	346 (13.0)	269 (11.5)
Total fat	1298 (48.8)	1257 (53.6)	960 (36.0)	791 (33.7)	404 (15.2)	292 (12.6)

* The sum of strata does not add up to the total because of some missing values.

controlled for using the Mantel–Haenszel procedure [23]. Significance was assessed by the linear trend test described by Mantel [24]. In order to account simultaneously for the effects of several potential confounding factors, unconditional multiple logistic regression was used [25]. Included in the regression equations were terms for age, area of residence, and the major identified or potential risk factors for breast cancer (e.g. education, history of benign breast disease and breast biopsies, history of breast cancer in mother or sister(s), nulliparity, age at first birth, age at menarche, menopausal status, age at menopause, body mass index, oral contraceptive and other female hormone use).

RESULTS

The distributions of cases and controls according to age, education and reproductive and menstrual factors are reported in Table 1. Compared to controls, cases were more highly educated and with older age at first birth and reported earlier menarche and later menopause.

The distribution of cases and controls according to intake

Table 3. Relative risks and 95% confidence intervals according to level of intake of various types of fat

Type of fat		Score			χ^2_1
		Low*	Intermediate	High	
Butter	M–H**	1	1.2 (1.1–1.4)	1.5 (1.1–1.9)	15.67 ⁺
	MLR‡	1	1.3 (1.1–1.5)	1.6 (1.2–2.1)	24.90 ⁺
Margarine	M–H**	1	1.0 (0.9–1.2)	1.1 (0.6–2.1)	N.S.
	MLR‡	1	1.0 (0.9–1.3)	1.3 (0.7–2.5)	N.S.
Oil	M–H**	1	1.2 (1.0–1.4)	1.3 (1.0–1.6)	5.10§
	MLR‡	1	1.1 (1.0–1.4)	1.2 (1.0–1.6)	3.37
Total fat	M–H**	1	1.2 (1.0–1.3)	1.4 (1.2–1.7)	15.76 ⁺
	MLR†	1	1.2 (1.0–1.4)	1.5 (1.2–1.7)	20.11 ⁺

* Reference category.

** Mantel–Haenszel estimates adjusted for age.

⁺ $P < 0.001$.

‡ Estimates from multiple logistic regression equations (see data analysis).

§ $P = 0.02$ and || $P = 0.07$.

of various seasoning fats is presented in Table 2, and the corresponding relative risks are given in Table 3. The highest RR emerged for high consumption of butter [the multivariate RR for the highest level was 1.6 (95% CI 1.2–2.1)], the trend in risk being highly significant (χ^2 for trend 24.90). Heavy consumption of margarine was reported by very few subjects and a non-significant elevation of breast cancer risk was found in this group [1.3 (0.7–2.5)]. The majority of study subjects described their consumption of oil as intermediate. Again, a moderate elevation in risk was observed in the highest tertile compared to the lowest one, of borderline statistical significance RR [1.2 (1.0–1.6)]. In relation to the summary seasoning fat score, compared to the highest level of intake, multivariate RRs were 1.2 (1.0–1.4) for the intermediate category and 1.5 (1.2–1.7) for the highest level. The trend in risk was, again, highly significant.

DISCUSSION

The results of this case-control study suggest that a positive association, although moderate, exists between breast cancer risk and intake of added fat in seasoning. Although not strong in absolute terms, this association applies to a substantial proportion of the female population (approximately half of the study subjects were in the intermediate and high categories of total fat intake), could not be explained by chance, and even after allowance for major identified potential confounding factors the trends in risk were statistically significant. There were only some suggestions for the association to be somewhat stronger for butter than for margarine or oil, but the relations were of similar direction and not formally heterogeneous for the various types of fats examined.

In consideration of its large dataset, statistical power and random variation are not a major problem in this study. More serious concerns derive from study design, which was of a typical hospital-based case-control investigation, with all the related strengths and weaknesses [22]. Although hospital controls may not be representative of the general population as concerns dietary habits, we specifically excluded all diagnoses related to digestive tract, or those which may have introduced long-term modifications in diet. Against selection bias, moreover, there are the practically complete participation rate and the comparable catchment area of cases and controls. With reference to confounding, the results were not appreciably modified by allowance for major breast cancer determinants. Further, both the subjects' distribution and the risk estimates were consistent between the first three years of data collection (1108 cases, 1281 controls, previously analysed in a general report of diet and breast cancer [11]) and in the subsequent 4 years. This repetition of similar results provides additional evidence on the observed association.

The most important problem of the present study, however, pertains to the type of information available on fat intake. In strict terms, with the data collected, inference can be made only on fat in seasoning, measured by simple subjective scores, and not validated. It is conceivable that these scores are an indicator, however indirect, of the subjects' attitude towards fats, and hence of their total fat intake, although this is clearly not quantifiable from available data. It is perhaps worth noting that in many traditional Italian dishes (e.g. pasta, green salads, boiled vegetables) seasoning fats are added, often uncooked, after food preparation, according to individual taste. Commercially prepared sauces and spreads are used very infrequently. The type and the quantity of fat in seasoning tends therefore to be readily recognisable and, as compared to other fat-rich foods

consumed less habitually, less subject to intraindividual variations and consequent measurement problems.

In relation to the other sources of fats investigated, the relative risks for subsequent tertiles of meat consumption, in the present dataset, were 1.3 (1.1–1.5) and 1.3 (1.1–1.5) (data not shown), and, although the interaction between various tertiles of fat in seasoning and meat was somewhat inconsistent, the risk estimate rose to 2.0 (1.5–2.6) in the highest meat/highest total seasoning fat category.

A further major limitation of this study is the absence of adequate estimation of total caloric intake, since fats are its major component and hence allowance for it may appreciably alter the relative risks for fats [26, 27].

With these cautions in mind, and the awareness of the data limitations, we still believe that the present findings may offer some, albeit indirect, contribution to an issue of major public health relevance. The results obtained are in broad agreement with overall evidence from 12 case-control studies recently reviewed [28] which showed relative risks of the order of 1.5 for both total and saturated fat, as well with a more recent large case-control study from Denmark, where the relative risk for the highest quartile of fat consumption was 1.45 [29]. Again, there was little definite evidence in those studies for a major role of saturated or mono-unsaturated fats, which represent the major component of olive oil (the most frequently consumed type of oil in Italy), although the relative risk for polyunsaturated fat was reduced in the model including simultaneously various types of fat [28].

Even if the increased risk for the upper levels of fat intake were of the order of 1.3–1.5, as found in this as well as other case-control (but not prospective) investigations, this would represent an association of similar magnitude to those observed for most well established reproductive and hormonal breast cancer risk factors [30] and would have major public health and prevention implications.

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Infections in Adults with Cancer in a Developing Country: a Three Year Prospective Study

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319 episodes of infections in 174 cancer patients over a period of 3 years are reported in a developing country. 178 episodes were seen in leukaemias, 83 in lymphomas and 58 in other cancers. 146 episodes appeared in 89 neutropenic patients and 173 in non-neutropenic patients. In 163 (51%) episodes positive cultures were obtained with a total of 212 organisms. 192 (90.6%) of the isolates were bacteria; of these 107 (55.7%) were gram positive and 85 (44.3%) were gram negative. The findings are consistent with those reported in developed countries. Most commonly isolated bacteria were: staphylococcus, *Escherichia coli*, streptococcus, enterobacter, pseudomonas, diphtheroids and salmonella. 15 isolates (7%) were of candida. Most common sites of infection were respiratory tract, kidney and urinary tract and skin. There were a total of 64 deaths: 36 were directly related to infections. 11 of these patients died of hospital acquired infections; most commonly isolated organisms in these infections were staphylococcus, *E. coli*, pseudomonas and streptococcus.

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INTRODUCTION

INFECTIONS ARE an important cause of death in patients with cancer and even more so in those with haematological malignancies [1]. In some series up to 64% of autopsied patients with acute leukaemia died from infections [2].

Infections in cancer patients result from the malignancy itself,

or from its treatment. The breakage of skin and mucosal barriers, impaired cell mediated immunity, impaired humoral immunity, intravenous lines and catheters and alteration of the body's normal microbial flora are all important predisposing factors [3]. The single most important of these factors is granulocytopenia [4]. Infection increases when granulocytes fall below $0.5 \times 10^9/l$. Serious infections and bacteraemias occur when granulocytes fall below $0.1 \times 10^9/l$ [5].

The aim of this work was to study prospectively over a period of three years the patterns of infections and organisms in a cancer unit in a developing country.

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