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Dietary fibres and ovarian cancer risk

C. Pelucchi[a,*], C. La Vecchia[a,b], L. Chatenoud[a], E. Negri[a], E. Conti[c], M. Montella[d], S. Calza[b], L. Dal Maso[e], S. Franceschi[f]

[a]*Istituto di Ricerche Farmacologiche "Mario Negri", 20157 Milan, Italy*
[b]*Istituto di Statistica Medica e Biometria, Università degli Studi di Milano, 20133 Milan, Italy*
[c]*Istituto Regina Elena per lo Studio e la Cura dei Tumori, 00143 Rome, Italy*
[d]*Istituto per lo Studio e la Cura dei Tumori "Senatore Pascale", 80100 Naples, Italy*
[e]*Servizio di Epidemiologia, Centro di Riferimento Oncologico, 33081 Aviano (PN), Italy*
[f]*Field and Intervention Studies Unit, International Agency for Research on Cancer, 69372 Lyon Cedex 08, France*

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Abstract

Data from an Italian multicentre case–control study on ovarian cancer were used to analyse the relationship between various types of fibres and ovarian cancer risk. The study, conducted between 1992 and 1999, included 1031 cases of incident, histologically-confirmed epithelial ovarian cancer. Controls were 2411 women admitted to the same network of hospitals for acute, non-malignant, non-hormonal-related diseases. Cases and controls were interviewed using a validated food frequency questionnaire (FFQ). Odds ratios (ORs), and the corresponding 95% confidence intervals (CI), were estimated using unconditional multiple logistic regression models. For total (Englyst) fibre, the OR for the highest versus the lowest quintile of intake was 0.68, and the continuous OR for the difference between the 80th and the 20th percentile of intake was 0.87. For most types of fibre, the continuous OR was significantly below 1. The OR was 0.83 for cellulose, 0.89 for soluble non-cellulose polysaccharides (NCPs), 0.86 for total insoluble fibre, 0.92 for insoluble NCP, and 0.95 (non-significant) for lignin. The inverse association was consistent across strata of age, family history and menopausal status, even if the association was apparently stronger in postmenopausal women. When fibre was classified according to the source, vegetable (but not grain) fibres, showed a significant protective effect, with an OR of 0.78.

Keywords: Diet; Fibre; Ovarian cancer; Epidemiology risk

1. Introduction

An inverse relationship between fibre intake and breast cancer risk has been reported from studies conducted in Canada [1], the Netherlands [2], Italy [3], Russia [4], Israel [5] and Australia [6], although the association was generally moderate, and no relation was observed in other studies [7,8]. The potential protection by fibres on breast carcinogenesis, if any, has been related to increased excretion and consequently lower serum oestrogen levels and/or increased production of lignans, or other phyto-oestrogens, which may reduce the availability of steroid hormones [9–11].

Ovarian cancer shares some, although not all, hormonal correlates of breast cancer [12,13]. Only limited data, however, are available on the potential relationship between fibre intake and ovarian cancer risk. A case–control study from Greece found a significant inverse relationship with crude fibres [14]. Other studies found inverse relationships between vegetables and fruit [15,16] or whole-grain food intake [17,18] and ovarian cancer risk, but this issue is still open to discussion.

We analysed, therefore, the relationship between various types of fibres and ovarian cancer risk, using data from the largest case–control study to date of diet and ovarian cancer [15].

2. Patients and methods

A multicentric case–control study of ovarian cancer was conducted between January 1992 and September 1999 in four Italian areas: the greater Milan area, the provinces of Pordenone, Padua and Gorizia in northern Italy, the province of Latina in central Italy, and the urban area of Naples in southern Italy [15].

* Corresponding author. Tel.: +39-02-39014-1; fax +39-02-33200-231.

E-mail address: pelucchi@marionegri.it (C. Pelucchi).

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Cases were 1031 women (median age 56 years, range 18–79 years) admitted to the major teaching and general hospitals in the areas under surveillance with incident, histologically-confirmed invasive epithelial ovarian cancer. Controls were 2411 women (median age 57 years, range 17–79 years) from the same catchment areas and admitted to the same network of hospitals as cases for acute, non-malignant and non-gynaecological conditions, unrelated to hormonal or digestive tract diseases or to long-term modifications of diet. Among controls, 26% were admitted for traumas, 28% for non-traumatic orthopaedic disorders, 15% for surgical conditions and 31% for miscellaneous other acute illnesses, such as eye, ear, nose, throat and dental disorders. Less than 4% of cases (3.4%) and controls (2.8%) approached refused the interview, and the response rate did not appreciably vary across geographical areas.

A standard questionnaire was administered by centrally trained interviewers during the hospital stay, including information on personal characteristics and lifestyle habits, a problem-oriented medical history, history of cancer in first-degree relatives, menstrual and reproductive factors, use of oral contraceptives (OC) and hormone replacement therapy.

An interviewer-administered food frequency questionnaire (FFQ) was developed to assess the usual diet during the 2 years preceding diagnosis (for cases) or hospital admission (for controls), in order to estimate the intake of total energy as well as that of selected nutrients. The questionnaire included 78 foods, food groups, or dishes divided into six sections: (1) bread, cereals, first courses; (2) second courses (i.e. meat, fish and other main dishes); (3) side dishes (i.e. vegetables); (4) fruits; (5) sweets, desserts and soft drinks; (6) milk, hot beverages and sweeteners.

For a few seasonal vegetables and fruits, consumption in season, and the corresponding duration were elicited. At the end of each section, one or two open questions were used to include foods that were not included in the questionnaire, but eaten at least once per week.

To compute energy and nutrient intake, Italian food composition databases were used, and integrated with other sources when needed [19]. The FFQ was satisfactorily reproducible [20] and valid [21]. Dietary fibre intake was derived using the Englyst procedure [22,23], which measures fibre as non-starch polysaccharides. A value was obtained for total fibre and for soluble and insoluble fibre. A modification of the method allows cellulose to be measured separately from insoluble non-cellulose polysaccharide (NCP). Values for lignin, a minor component of the human diet, were provided separately. We did not include resistant starch in the computation of total fibre, because the amount depends on how each food is processed and consumed [24], and related food composition tables were not available. Fibre intake was also divided according to the food from which it originated (i.e. vegetable, fruit or cereal).

2.1. Data analysis

Odds ratios (OR) of ovarian cancer and the corresponding 95% confidence intervals (CI) for various measures of fibre intake were derived using unconditional multiple logistic regression, fitted by the method of maximum likelihood [25]. All regression equations included terms for study centre, quinquennia of age, education (<7, 7–11, ≥ 12 years), occupational physical activity, parity, OC use, family history of ovarian and/or breast cancer in first-degree relatives, and menopausal status. Intake for various fibres was computed on the regression on energy, following the method suggested by Willett and Stampfer [26]. Various types of fibres were also introduced in the model as continuous variables. Wald's test was used to assess the significance of the coefficients for continuous variables.

3. Results

Table 1 gives the distribution of cases and controls according to age, education and parity. Ovarian cancer cases had a similar age distribution as controls, and were significantly more educated, with an OR of 1.88 for 12 years or more; cases reported lower parity than controls (OR = 0.62 for 3, 0.38 for 4 and 0.41 for ≥ 5 births), and more frequently had a family history of ovarian or breast cancer (OR = 2.64).

Table 2 gives the distribution of ovarian cancer cases and controls, the ORs (in quintiles and continuously) and the test for trend for various types of fibres after allowance for energy intake and other potential confounding factors. ORs were significantly below unity for the highest intake quintiles of soluble NCP (OR = 0.75), cellulose (OR = 0.69), total insoluble fibres (OR = 0.70) and total fibre (OR = 0.68). The OR was 0.78 for insoluble NCP and 0.84 for lignin (non-significant). The ORs in continuous, using as a measurement unit the difference between the upper cut-point of the fourth and first quintile (80th and 20th percentiles), varied between 0.83 for cellulose and 0.95 for lignin. Most tests for linear trend were also significant, except that for lignin. With reference to the source of fibre, we found an inverse association with vegetable fibre (OR = 0.59 for the highest quintile), while grain fibre appeared to be directly associated (OR = 1.32). No clear relationship emerged for fruit fibre.

Table 3 shows the continuous ORs, according to total fibre, in separate strata of parity, menopausal status and family history of ovarian or breast cancer. No appreciable or significant heterogeneity emerged across various strata, although the inverse relationship between total fibre intake and ovarian cancer risk appeared stronger in post- (OR = 0.81) compared with pre-menopausal women (OR = 0.97).

4. Discussion

The present study, based on a uniquely large dataset, a comprehensive FFQ and estimates of intakes for various types of fibre, found an inverse relationship between fibre consumption and ovarian cancer risk. The association was consistent across strata of covariates but, as for other selected dietary factors [15], was apparently stronger in post-menopausal women. The protection was observed for various types of fibre, including soluble and insoluble fibre, lignin, and vegetable fibre. This may reflect the positive correlation between various types of fibre, as well as the inverse relationship between selected foods, including raw and cooked vegetables, and ovarian cancer risk [15].

In the same population, an inverse relationship was observed between fibre intake and cancers of the upper digestive tract [27], and of the colorectum [29], and a moderate favourable effect was also observed for breast cancer [3]. Likewise, several other studies of fibres and breast cancer have found moderate inverse relationships [1,2,5], and a significant inverse association was observed in a case–control study of endometrial cancer in the USA [30].

Table 1
Distribution of 1031 cases of epithelial ovarian cancer and 2411 controls according to age and selected characteristics. Italy, 1992–1999

	Cases		Controls		OR (95% CI)[a]
	n	(%)	*n*	(%)	
Age (years)					
<45	183	(17.7)	443	(18.4)	–
45–54	287	(27.8)	615	(25.5)	–
55–64	325	(31.5)	724	(30.0)	–
⩾65	236	(22.9)	629	(26.1)	–
Education (years)[b]					
⩽6	570	(55.7)	1417	(59.4)	1[c]
7–11	227	(22.2)	620	(26.0)	1.09 (0.88–1.36)
⩾12	227	(22.2)	349	(14.6)	1.88 (1.47–2.41)
Parity					
0	184	(17.8)	381	(15.8)	1[c]
1	196	(19.0)	473	(19.6)	1.07 (0.80–1.43)
2	376	(36.5)	794	(32.9)	0.90 (0.69–1.16)
3	175	(17.0)	454	(18.8)	0.62 (0.46–0.83)
4	54	(5.2)	185	(7.7)	0.38 (0.25–0.58)
⩾5	46	(4.5)	124	(5.1)	0.41 (0.26–0.66)
Menopausal status[b]					
Pre–in	346	(33.6)	803	(33.4)	1[c]
Post	683	(66.4)	1603	(66.6)	1.02 (0.78-1.37)
Family history of ovarian and/or breast cancer					
No	902	(87.5)	2291	(95.0)	1[c]
Yes	129	(12.5)	120	(5.0)	2.64 (1.99–3.54)

OR, odds ratio; 95% CI, 95% confidence interval.

[a] Estimates from multiple logistic regression including terms for age, centre and year of interview.

[b] The sum does not add up to the total because of some missing values.

[c] Reference category.

The inverse relationship between fibre and ovarian cancer risk may be related to changes in bacterial macroflora, increased excretion and consequently lower serum levels and availability of oestrogens, and increased protection of lignans or other phyto-oestrogens [31], which may reduce the bioavailability of steroid hormones, which in turn are related to ovarian carcinogenesis. Fibre, moreover, may reduce glycaemic load [32] and improve insulin sensitivity, favourably influencing insulin-like growth factor 1 (IGF-1), which is a promoter of the process of carcinogenesis at various (hormone-related) sites [33]. This applies particularly to soluble fibre, which are the most effective type in delaying starch absorption.

In the Italian population, the cereals consumed are mostly refined grains, leading to a high ratio between starch and fibre intake. Consequently, the potential promotional action of starch [34] may overwhelm any possible protective action of fibre.

As observed in a companion study of colorectal cancer [28], the protections conferred by cellulose and soluble NCPs seem somewhat stronger than those of insoluble NCPs and lignin. However, plant foods contain various types of fibre together, and the intakes of various types of fibre were positively correlated. This makes it difficult to distinguish between their separate effects.

Moreover, it is unclear whether the apparent inverse relationship between fibre and ovarian cancer reflects other aspects of diet composition, which are difficult to completely allow for in the analysis; for instance, high fibre diets tend to have also a high content of antioxidant vitamins, and are generally richer of vegetables, fruit and the related wide spectrum of substances with a potentially favourable influence on the process of carcinogenesis [35]. This study, in fact, found that fibres from vegetables (but not those from cereals) protect against ovarian cancer. It is, however, unclear whether other components of a diet rich in vegetables are the major underlying determinant of their protection, and reciprocal allowance of various factors or cofactors is hampered by inherent problems of collinearity.

With reference to potential sources of bias, dietary habits of hospital controls may differ from those of the general population, but we excluded from the control group all diagnoses that might have involved long-term modification of diet, and separate comparison of cases with the main diagnostic categories of controls yielded comparable results. The potential relationship between fibres and ovarian cancer has not gained widespread attention in Italy, and it is therefore unlikely to have caused differential recall in cases and controls. Among

Table 2
Odds ratios[a,b] (OR) and 95% confidence intervals (CI) of ovarian cancer according to the intake of various types of fibre, Italy 1992–1999

Type of fibre	Quintile of intake[c]				Trend χ^2	Continuous OR (95% CI)[d]
	Q2	Q3	Q4	Q5		
Total (Englyst) fibre	(11.51)	(14.44)	(17.30)	(21.05)		
OR (95% CI)	0.91 (0.71–1.17)	0.86 (0.67–1.11)	0.84 (0.66–1.08)	0.68 (0.53–0.88)	8.5**	0.87 (0.78–0.98)
Soluble NCP	(5.69)	(7.05)	(8.40)	(10.08)		
OR (95% CI)	0.85 (0.66–1.09)	0.81 (0.63-1.05)	0.78 (0.61–1.00)	0.75 (0.58–0.96)	5.7*	0.89 (0.80–0.99)
Total insoluble fibre	(5.75)	(7.37)	(8.89)	(10.90)		
OR (95% CI)	0.93 (0.72-1.19)	0.85 (0.66-1.09)	0.77 (0.60-0.99)	0.70 (0.54–0.89)	10.1**	0.86 (0.77-0.97)
Cellulose	(2.94)	(3.84)	(4.67)	(5.80)		
OR (95% CI)	0.86 (0.67-1.10)	0.78 (0.61-1.01)	0.64 (0.49-0.82)	0.69 (0.54–0.88)	13.2**	0.83 (0.74-0.93)
Insoluble NCP	(2.76)	(3.47)	(4.19)	(5.14)		
OR (95% CI)	0.99 (0.77–1.27)	1.07 (0.83–1.38)	0.88 (0.68–1.13)	0.78 (0.60–1.01)	4.4*	0.92 (0.84–1.02)
Lignin	(1.06)	(1.34)	(1.59)	(1.96)		
OR (95% CI)	1.04 (0.81–1.34)	0.95 (0.74–1.23)	1.07 (0.83–1.37)	0.84 (0.65–1.09)	1.1	0.95 (0.85–1.06)
Vegetable fibre	(3.79)	(5.00)	(6.14)	(7.80)		
OR (95% CI)	0.88 (0.69–1.13)	0.80 (0.62–1.02)	0.72 (0.56–0.92)	0.59 (0.46–0.77)	18.2**	0.78 (0.69–0.88)
Fruit fibre	(3.20)	(4.95)	(6.40)	(8.81)		
OR (95% CI)	0.98 (0.76–1.25)	0.91 (0.70–1.17)	0.78 (0.60–1.00)	0.96 (0.75–1.22)	1.1	0.94 (0.85-1.04)
Grain fibre	(2.83)	(3.66)	(4.43)	(5.52)		
OR (95% CI)	1.09 (0.84–1.42)	1.16 (0.89–1.50)	1.34 (1.03–1.73)	1.32 (1.03–1.71)	6.6**	1.06 (0.98-1.14)

NCP, non-cellulose polysaccharides. *$P < 0.05$; **$P < 0.01$.
[a] Estimates from multiple logistic regression including terms for quinquennia of age, centre, education, occupational physical activity, parity, oral contraceptive use, family history of ovarian and/or breast cancer in first-degree relatives, menopausal status and total energy intake.
[b] Quintiles are computed on the distribution of controls. In parentheses is given the lower cut-point of the quintile in g/day.
[c] The reference category is the first (lowest) quintile.
[d] The unit is the difference between the 80th and 20th percentile, i.e. between the upper cut-points of the fourth and first quintiles.

Table 3
Odds ratios (OR) and 95% confidence intervals (CI) of epithelial ovarian cancer according to total fibre intake, in separate strata of selected covariates, Italy, 1992–1999

Covariate	Continuous OR (95% CI)[a]
Parity	
<3	0.92 (0.81–1.05)
⩾3	0.77 (0.61–0.97)
Menopausal status	
Pre–peri	0.97 (0.81–1.16)
Post	0.81 (0.70–0.94)
Family history of ovarian and/or breast cancer	
No	0.87 (0.77–0.98)
Yes	0.94 (0.62–1.42)

[a] Estimates from multiple logistic regression including terms for quinquennia of age, centre, education, occupational physical activity, parity, oral contraceptive use, family history of ovarian and/or breast cancer in first-degree relatives, menopausal status and total energy intake. The unit for fibre intake is the difference between the 80th and 20th percentiles of the distribution of controls, i.e. between the upper cut-points of the fourth and first quintiles.

other strengths of this study, there are the satisfactory reproducibility and validity of the FFQ: the adjusted Pearson correlation coefficents for reproducibility were 0.62 for starch and 0.67 for fibres [20]. Corresponding values for validity were 0.60 for starch and 0.57 for fibres [21]. Furthermore, among the strengths of this study there are the comparable catchment areas of cases and controls, the practically complete participation, and the possibility of allowance for several relevant covariates, including total energy intake, in the analysis [26]. More importantly, this study included detailed information on the various types of fibre, and was large enough to allow precise quantification of even moderate effects.

In conclusion, therefore, this study indicates that several sources of dietary fibre may exert a moderate, but significant, protection on ovarian cancer risk, and suggests that the inverse relationship may be stronger in post-menopausal women. It also confirms that various types of fibre should be considered separately, since their role may be different in the process of hormone-related carcinogenesis.

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