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Short communication

Allium vegetables intake and endometrial cancer risk

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Abstract

Objective: The potential role of allium vegetables on endometrial cancer risk has been scarcely investigated and the results of previous Chinese studies are not easily applicable to Western populations. Therefore, we evaluated the relationship between onion and garlic intake and endometrial cancer, using data from an Italian case–control study.

Setting: We analysed data from a multi-centre case–control study of 454 endometrial cancer cases and 908 controls, admitted to the same hospitals for a wide spectrum of acute, non-neoplastic conditions. Information was collected by trained interviewers using a validated and reproducible FFQ. Multivariate odds ratios and 95 % confidence intervals were obtained after allowance for recognized confounding factors.

Results: Compared with non-users, the OR of endometrial cancer for successive categories of onion intake were 0·94 (95 % CI 0·72, 1·21) for <2 portions/week and 0·40 (95 % CI 0·22, 0·72) for ≥2 portions/week, with a significant inverse trend in risk ($P = 0·01$). The OR for an increment of one portion (i.e. 80 g) of onions per week was 0·81 (95 % CI 0·70, 0·95). For garlic, the OR for successive categories of intake were 0·89 (95 % CI 0·68, 1·15) for intermediate use and 0·62 (95 % CI 0·42, 0·92) for high use, with a significant inverse trend in risk ($P = 0·02$).

Conclusions: Our study found a moderate protective role of allium vegetables on the risk of endometrial cancer.

Keywords
Allium vegetables
Diet
Endometrial cancer
Garlic
Onion
Risk factors

Several epidemiological studies have found that diet may influence endometrial cancer independently from obesity, which is an established risk factor that acts by increasing oestrogen[1,2]. However, the evidence for the role of specific foods or food groups is limited and controversial[1]. Several investigations reported an inverse relationship with vegetables and fruit intake, but these findings are not consistent[3–6]. To our knowledge, the potential role of allium vegetables on endometrial cancer risk has been investigated in only two case–control studies among Chinese women in Shanghai[3,4]. The first study was conducted among 268 cases and 268 controls and found a moderate non-significant inverse association between allium vegetables intake and endometrial cancer risk[3]. The second study was conducted among 832 cases and 846 controls and found an OR of 0·76 (95 % CI 0·56, 1·03) for the highest *v.* the lowest quartile of allium vegetables intake, with a significant trend in risk ($P = 0·04$)[4]. The inverse association was appreciably stronger in premenopausal women, with an OR of 0·41 (95 % CI 0·24, 0·71) for the highest *v.* the lowest quartile of intake ($P < 0·01$).

The results of these studies are not easily applicable to Western populations, whose dietary habits are largely different and in particular whose garlic intake is far lower[7]. Therefore, we evaluated the relationship between onion and garlic intake and endometrial cancer, using data from a multi-centre case–control study conducted in Italy.

Materials and methods

A case–control study on endometrial cancer was conducted between 1992 and 2006 in three Italian areas, including greater Milan, the provinces of Udine and Pordenone in northern Italy and the urban area of Naples in southern Italy. Cases were 454 women (median age 60 years, range 18–79 years) with incident, histologically confirmed endometrial cancer (code 182.0 in the *International Classification of Diseases*, 9th revision), admitted

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to major teaching and general hospitals of the study areas. Controls were 908 women (median age 61 years, range 19–80 years) admitted to the same hospitals as cases for a wide spectrum of acute non-neoplastic conditions. Controls were matched with cases by quinquennia of age and study centre, with a case to control ratio of 1:2. Thirty-six per cent of controls were admitted for traumas, 32% for other orthopaedic disorders, 9% for acute surgical conditions and 23% for miscellaneous other illnesses, including eye, nose, ear, skin or dental disorders.

Interviewers used a structured questionnaire to gather information on sociodemographic factors, anthropometric variables, smoking, alcohol and other lifestyle habits, problem-oriented medical history, physical activity and history of cancer in first-degree relatives. Information on diet referred to the 2 years preceding diagnosis and was based on an FFQ that had previously been tested for reproducibility and validity[8,9]. The FFQ included seventy-eight foods, food groups or recipes, and allowed an estimation of energy intake. Among the items in the FFQ, two questions referred specifically to the consumption of onion and garlic. For onion intake, we asked for the weekly frequency of consumption and usual portion size (small, intermediate, large), where an intermediate portion corresponded to 80 g of onion. A small portion was considered as 0·7 times an intermediate portion, and a large portion was considered as 1·3 times an intermediate portion. Frequencies of less than once per week, but at least once per month, were coded as 0·5 per week. For frequency of garlic use, we asked for the common consumption as a qualitative variable, scored as 1 for non-use or low use, 2 for intermediate use and 3 for high use. No additional information on the type of garlic and onion consumed or on manner of use (fresh, powders or garlic supplements) was available.

To compare cases and controls according to selected anthropometric and dietary variables, we used a two-sided χ^2 test for categorical variables, a two-sided Student's t test for approximately normally distributed variables (based on the Shapiro–Wilk statistic) and a two-sided Wilcoxon's rank-sum test otherwise.

The odds ratio and the corresponding 95% confidence intervals for different levels of onion intake (non-users; infrequent users, >0 to <2 portions/week; frequent users, ≥2 portions/week) and garlic use (none or low, intermediate, high) were derived using multiple logistic regression models stratified for study centre and quinquennia of age, and adjusted for years of education, total energy intake, BMI, age at menarche, parity, oral contraceptive and hormone replacement therapy use, and menopausal status[10].

Results

Table 1 shows the distribution of 454 cases of endometrial cancer and 908 controls according to age, personal and lifestyle characteristics and selected dietary factors. BMI and energy intake of cases were higher than those of controls ($P < 0{\cdot}0001$ and $P = 0{\cdot}015$, respectively). Cases consumed total vegetables, onions and garlic less frequently than controls, even if these differences were not statistically significant.

Table 2 reports the distribution of endometrial cancer cases and controls, the OR and 95% CI for successive levels of onion intake and garlic use. Compared with non-users, the crude OR of endometrial cancer cases for successive categories of onion intake were 0·99 (95% CI 0·78, 1·26) for <2 portions/week and 0·56 (95% CI 0·33, 0·93) for ≥2 portions/week. The corresponding multivariate OR were 0·94 (95% CI 0·72, 1·21) and 0·40 (95% CI 0·22, 0·72), with a significant inverse trend in risk ($P = 0{\cdot}01$). The multivariate OR for an increment of one portion of onions per week (i.e. 80 g/week) was 0·81 (95% CI 0·70, 0·95). For garlic, the crude OR for successive categories of intake were 0·98 (95% CI 0·78, 1·24) for intermediate use and 0·73 (95% CI 0·51, 1·02) for high use, as compared with non-/low users. The corresponding multivariate OR were 0·89 (95% CI 0·68, 1·15) and 0·62 (95% CI 0·42, 0·92), with a significant inverse trend in risk ($P = 0{\cdot}02$). We also considered the OR in separate strata of age, education, BMI and, for garlic, intake of lipids, proteins and cruciferous vegetables. No significant heterogeneity emerged across any of the strata considered (data not shown).

Discussion

Epidemiological studies suggest that allium vegetable intake reduces the risk of cancer and laboratory investigations have provided convincing evidence that selected substances contained in garlic and other allium vegetables inhibit a variety of chemically induced tumours in animals[7,11,12]. The protective effect appears to be related to the presence of organosulfur compounds, mainly allyl derivates, which inhibit proliferation of human digestive tract, mammary, endometrial and colon cancer cells[11,13]. Although the exact preventive mechanisms on cancer are not clear, several hypotheses have been proposed. These include modulation of the activity of several metabolizing enzymes that activate and detoxify carcinogens and inhibit DNA adduct formation, antioxidant and free radicals scavenging properties, and regulation of cell proliferation, apoptosis and immune responses[14]. Moreover, several studies have reported the antihypertensive effect of garlic[15], and hypertension has been directly associated with endometrial cancer risk[1,16].

However, onion and garlic intake in Italy could also be simply considered markers of a healthier lifestyle, which may include complex aspects of quantity and quality of the diet, and in particular of a diet rich in vegetables that has been inversely associated with endometrial cancer[17]. In fact, in the Italian diet, onion and garlic are

Table 1 Frequency distribution of 454 endometrial cancer cases and 908 controls according to relevant covariates and information on selected dietary aspects, Italy, 1992–2006

	Cases		Controls		
	n or Mean	% or SD	*n* or Mean	% or SD	*P**
Age (years)					
<50	67	15	134	15	–
50–59	140	31	280	31	
60–69	166	36	332	36	
≥70	81	18	162	18	
Education (years)					
<7	263	58	553	61	0·55
7–11	119	26	225	25	
≥12	72	16	130	14	
Age at menarche (years)†					
<11	24	5	44	5	0·001
11–13	283	63	475	53	
14–16	137	30	345	38	
≥17	8	2	38	4	
Parity					
Nulliparous	68	15	126	14	0·58
Parous	386	85	782	86	
Oral contraceptive use					
Never	408	90	790	87	0·13
Ever	46	10	118	13	
Hormone replacement therapy					
Never	405	89	830	91	0·19
Ever	49	11	78	9	
Menopausal status†					
Pre-/perimenopausal	85	19	174	19	0·95
Postmenopausal	358	81	726	81	
BMI (kg/m^2)	28·8	6·2	25·8	4·2	<0·0001
Energy intake (kJ/d)	9182	2805	8817	2576	0·015
Energy intake (kcal/d)	2193	670	2106	614	0·015
Total vegetable intake (portions/week)	11·8	6·9	12·2	6·0	0·051
Onion intake (portions/week)	0·4	0·8	0·5	1·0	0·412
Garlic use (intake score)	1·7	0·7	1·7	0·9	0·222

*Calculated using the χ^2 test for education, age at menarche, parity, oral contraceptive use, hormone replacement therapy use and menopausal status; the two-sided Student's *t* test for BMI and energy intake; and the two-sided Wilcoxon rank-sum test for other variables.
†Sum did not equal total because of some missing values.

Table 2 Distribution of 454 endometrial cancer cases and 908 controls and odds ratios* and 95 % confidence intervals according to onion intake (portions/week) and garlic use, Italy, 1992–2006

	Cases:controls	OR	95 % CI
Onion intake (portions/week)			
Non-users	265:511	1·00§	–
>0 to <2	169:328	0·94	0·72, 1·21
≥2	20:69	0·40	0·22, 0·72
P for trend		0·01	
Continuous OR†		0·81	0·70, 0·95
Garlic use‡			
None or low	197:376	1·00§	–
Intermediate	204:393	0·89	0·68, 1·15
High	53:138	0·62	0·42, 0·92
P for trend		0·02	

*Estimates from logistic regression, stratified for age and centre, and adjusted for total energy intake, education, BMI, age at menarche, parity, oral contraceptive use, hormone replacement therapy use and menopausal status.
†OR for an increment of one portion (80 g) per week.
‡The sum does not add up to the total because of some missing values.
§Reference category.

often eaten or cooked in combination with other foods, such as tomatoes and olive oil in salads and tomato sauces for pasta.

Among the limitations of the present study, selection and recall biases are possible. A recent cancer diagnosis might have influenced recall of diet for cases, although awareness of dietary hypotheses for endometrial cancer is limited among the general population and the interviewers. Further, by interviewing subjects in the same hospital setting, the comparability of information between cases and controls is improved[18]. Patients hospitalized for chronic or digestive tract conditions were excluded. We collected no information on the variety of onions and type of garlic used and on modalities of cooking; nor on the intake of other allium vegetables, such as scallions and chives, which were inversely related to endometrial cancer risk in a Chinese study[4,19]; nor on genetic polymorphisms that may be involved in endometrial cancer.

Major strengths of the present study are its large size combined with the collection of extensive dietary information using a satisfactorily reproducible and valid FFQ[8,9], the comparable catchment areas of cases and controls, the high participation rate and the possibility of allowance for intake of energy and for several covariates in the analyses. Thus, we were able to allow in the analysis for selected major lifestyle and nutritional factors, including

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physical activity, vegetable and fruit consumption, but the multivariate OR were not appreciably modified. The Spearman correlation coefficient for reproducibility of frequency of onion intake was 0·48, and the concordance of the subjective question on garlic use was highly reproducible in 70–80 % of the subjects[9].

Our study, the first from a Western country, found a moderate protective role of allium vegetables on the risk of endometrial cancer, supporting previous findings reported among Chinese populations.

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