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Frequent Consumption of Vegetables and The Decreased Risk of Ovarian Cancer

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ABSTRACT

A case-control study was conducted to assess the relationship of dietary habits to ovarian cancer. A uniform questionnaire was filled out by 44 ovarian cancer cases hospitalized at Sapporo Medical University or 2 other hospitals in Sapporo between August and norember, 1990. Two hundred twenty individually locality-matched controls were selected from telephone books and sent the same questionnaire; 156 (70.9%) responded. The conditional logistic regression analysis was used to compare the data of 44 ovarian cancer cases and the 156 individually age-matched controls. Univariate analysis revealed that single marital status was significantly associated with the increased risk of ovarian cancer (odds ratio, or OR=3.45, 95% confidence interval, or 95%CI 1.13-10.84). Frequent intake of midnight meals was also significantly related to the increased risk (trend, OR=1.56, 95%CI 1.01-2.41), and frequent intake of vegetables other than yellow or red was significantly related to the decreased risk (trend, OR=0.58, 95%CI 0.37-0.91). These odds ratios concerning dietary habits were not substantially altered even after adjustment for potentially distorting variables such as marital status, the number of parities, and family history for uterine, ovarian, or breast cancer with the multivariate analysis. No other dietary habits, including frequent consumption of meat, fish, or milk, were associated with the increase or decrease of the risk of ovarian cancer.

Key words: Ovarian neoplasms, Case-control studies, Risk factors, Dietary habits, Vegetables

INTRODUCTION

We have suggented that some reproductive and genetic factors are associated with the risk for ovarian cancer[1]. Nulliparity and family history of breast or

ovarian cancer are well known examples of risk factors, while the role of dietary habits has been less clearly elucidated.

The incidence of ovarian cancer has been gradually rising in Japan[2], and it is speculated that some environmental factors, especially recent changes in dietary habits, could be associated with the increasing incidence of ovarian cancer in Japan. Accordingly, we conducted a case-cantrol study to assess the relation of dietary factors to ovarian cancer in Sapporo.

SUBJECTS AND METHODS

Ovarian cancer cases aged over 18 years and under 79 years were identified from inpatients or outpatients at Sapporo Medical University and 2 other hospitals in Sapporo in the time period of August, 1990 to October, 1990. Information on dietary habits for about 5 years previous to the time when the initial symptom had been noted. Marital status, number of parities, family history for cancer, and other factors were collected by a uniform questionnaire filled out by the patients themselves.

Five controls per case were randomly selected from the telephone books for Hokkaido; the five were selected from the same administrative region (city or county) as each corresponding case. These women were sent the same questionnaire as used for the case group in November, 1990 with a letter which explained the object of the study. It asked that a woman between the ages of 18 and 79 years fill out the questionnaire. If there was no response to our first request, a second letter was sent to the non-respondent family along with another copy of the questionnaire.

After the questionnaires were returned from the control women, data sets were established from the ovarian cancer cases and the respondents, the number of whom varied from 2 to 5 per case, by matching each control's age with a case (within 5 years). Conditional logistic regression analysis was executed for the data of the ovarian cancer cases and the individually age-matched controls[3]. SAS Software was utilized for the analysis[4].

RESULTS

Forty-four ovarian cancer cases were identified during the study period, and all of them responded to the survey. The average age was 50.2 (the standard deviation, or SD=13.3) years, and 33 of them (75.0%) were diagnosed within 2 years before the survey. Their pathological diagnoses were confirmed as shown in Table 1.

Of the 220 families (5 per case) selected randomly, 118 and 38 women in those families responded to our first and second requests, respectively, for a total

response rate of 70.9%. Their average age was 48.2 (SD=12.8) years. Forty-four data sets of cases and individually age-matched controls were established as follows: 7 sets of 2-to-1 matching; 17 sets of 3-to-1 matching; 9 sets of 4-to-1 matching; and 11 sets of 5-to-1 matching.

As shown in Table 2, univariate analysis revealed that single marital status was significantly associated with the increased risk of ovarian cancer (odds ratio, or OR=3.45, 95% confidence interval, or 95%CI 1.13-10.84). The number of parities were slightly inversely related to the risk of ovarian cancer (trend, OR=0.91, 95%CI 0.69-1.18), and occurrence of family history for uterine, ovarian, or breast cancer was positively related to the risk of ovarian cancer (OR=1.76, 95%CI 0.80-3.86), although neither of them were statistically significant.

Table 1. *Pathological classification of ovarian cancer*

Type	No.
serous (papillary) (cyst) adenocarcinoma	20
mucinous (cyst) adenocarcinoma	9
clear cell carcinoma	5
endometrioid carcinoma	2
poorly differentiated carcinoma	1
(papillary) adenocarcinoma	3
mixed germ cell-stromal tumor	1
embryonal carcinoma	1
yolk sac tumor with choriocarcinoma	1
anaplastic seminoma	1
Total	44

Table 2. *Odds ratio (OR) and its 95% confidence interval (95% CI) for items other than dietary habits.*

Item	Unit	OR	95%CI
Body height	cm	1.00	0.98- 1.02
Body weight	kg	0.98	0.94- 1.02
BMI	kg/m^2	0.92	0.83- 1.02
Marital status: Single	yes/no	3.45	1.13-10.84
Nulliparous	yes/no	1.86	0.80- 4.31
Parity	number	0.91	0.69- 1.18
Occupation: Clerical work	yes/no	0.71	0.23- 2.13
Father's occupation: Agriculture	yes/no	0.63	0.22- 1.75
Family history: Uterine cancer	yes/no	1.61	0.60- 4.32
Family history: Ovarian cancer	yes/no	2.59	0.43-15.65
Family history: Breast cancer	yes/no	1.80	0.62- 5.23
Family history: Uterine, ovarian, or breast cancer	yes/no	1.76	0.80- 3.86

As shown in Table 3, frequent intake of midnight meals was significantly related to the increased risk of ovarian cancer (trend, OR=1.56, 95%CI 1.01-2.41), and the frequent intake of vegetables other than yellow or red, to the decreased risk of ovarian cancer (trend, OR=0.58, 95%CI 0.37-0.91). No other dietary habits, including frequent consumption of meat, fish, eggs, milk, green or yellow vegetables, or fruits, were significantly associated with the increase or decrease of the risk of ovarian cancer.

The correlation coefficients were calculated among the factors possibly as-

Table 3 *Odds ratio (OR) and its 95% confidence interval (CI) for dietary habits with the univariate analysis.*

Item	Unit	OR	95%CI
Skipping breakfast or lunch	frequency*)	1.19	0.71-1.99
Not considering a variety of foods	frequency*)	1.40	0.85-2.29
Irregular meal times	frequency*)	1.63	0.95-2.80
Intake of midnight meals	frequency**)	1.56	1.01-2.41
Intake of between-meal snacks	frequency†)	0.77	0.56-1.04
Consumption of instant food	frequency**)	0.82	0.38-1.79
Consumption of cooked food	frequency†)	0.95	0.55-1.63
Eating out	frequency†)	1.05	0.60-1.86
Consumption of Rice	frequency§)	0.96	0.56-1.63
Consumption of Meat	frequency†)	0.94	0.57-1.53
Favorite meat: Pork	yes/no	0.75	0.38-1.45
Favorite meat: Beef	yes/no	1.06	0.34-3.27
Favorite meat: Chicken	yes/no	1.28	0.61-2.69
Frequent consumption of hamburger	yes/no	0.62	0.27-1.45
Frequent consumption of cutlet	yes/no	1.04	0.50-2.17
Consumption of fat portions	frequency*)	0.96	0.55-1.67
Consumption of fish	frequency†)	0.64	0.40-1.02
Consumption of eggs	frequency†)	0.80	0.53-1.18
Consumption of tofu or soy beans	frequency†)	1.00	0.66-1.52
Consumption of milk	frequency†)	1.04	0.80-1.34
Consumption of seaweeds	frequency†)	0.82	0.50-1.35
Consumption of yellow or red vegetables	frequency†)	1.31	0.85-2.02
Consumption of vegetables other than yellow or red	frequency†)	0.58	0.37-0.91
Consumption of fruits	frequency†)	0.83	0.56-1.21
Consumption of mayonnaise or dressing	frequency†)	1.08	0.72-1.60
Consumption of oil-cooked foods	frequency†)	0.72	0.44-1.16
Consumption of sweets	frequency†)	0.64	0.36-1.16

*): 1. never 2. sometimes 3. frequent

**): 1. seldom 2. 1-2 times/week 3. 3-5 times/week 4. every day

†): 1. seldom 2. 1-2 times/week 3. 3-5 times/week 4. every day 5. more than once/day

§): 1. seldom 2. once/day 3. twice/day 4. 3 times/day 5. more than 3 times/day

sociated with the risk of ovarian cancer. As shown in Table 4, the frequent intake of vegetables other than yellow or red was significantly negatively correlated to single marital status (correlation coefficient, or $r=-0.341$, $P<0.05$) and to family history for uterine, ovarian or breast cancer ($r=-0.339$, $P<0.05$) in the case group. In both the case and control groups, the number of parities

Table 4. *Correlation coefficient matrix of factors possibly associated with the increase or decrease of the risk for ovarian cancer.*

The Case Group					
	Marital status: Single	The number of parities	Family History	Intake of midnight meals	Intake of yellow or red vegetables
Marital status: Single	1.000				
The number of parities	−0.635***	1.000			
Family history†)	0.340*	−0.088	1.000		
Intake of midnight meals§)	−0.142	−0.107	0.070	1.000	
Taking yellow or red vegetables§)	−0.225	0.034	−0.209	0.050	1.000
Taking vegetables other than yellow or red§)	−0.341*	0.011	−0.339*	0.231	0.488***
The Control Group					
	Marital status: Single	The number of parities	Family History	Intake of midnight meals	Intake of yellow or red vegetables
Single marital status	1.000				
The number of parities	−0.439***	1.000			
Family history†)	−0.019	0.060	1.000		
Intake of midnight meals§)	−0.128	0.104	0.142	1.000	
Intake of yellow or red vegetables§)	−0.090	0.070	0.076	−0.099	1.000
Intake of vegetables other than yellow or red§)	−0.018	0.154	0.062	−0.044	0.481***

†): Family history of uterine, ovarian or breast cancer.
§): Frequency (See Table 3)
***: $p<0.001$ *: $P<0.05$

was significantly negatively correlated to single marital status ($P<0.001$), and the frequent intake of yellow or red vegetables significantly positively correlated to the frequent intake of vegetables other than yellow or red ($P<0.001$).

Adjusted odds ratios for various dietary habits were computed after the potentially confounding variables such as marital status, number of parities, and family history for uterine, ovarian, or breast cancer were simultaneously included in the model, which was then subjected to multivariate conditional logistic analysis. As shown in Table 5, the frequent intake of midnight meals was still significantly related to the increased risk of ovarian cancer (trend, OR=1.67, 95%CI 1.04-2.76), and the frequent intake of vegetables other than yellow or red was also still significantly associated with the decreased risk of ovarian cancer (trend, OR=0.61, 95%CI 0.37-0.99).

DISCUSSION

According to the correlational study by Rose et al.[5], caloric intake from vegetable sources was strongly negatively correlated to the age-adjusted mortality rates of ovarian cancer, while caloric intake from animal sources was positively correlated. After a case control study in Italy, Negri *et al*[6] have shown that frequent consumption of vegetables was significantly associated with the decreased risk of ovarian cancer. Cramer *et al.*[7] found in a case-control study that women with ovarian cancer consumed significantly less vegetable fat

Table 5. *Odds ratio (OR) and its 95% confidence interval (CI) for dietary factors which are related to ovarian cancer risk.*

Item	Case	Control	OR*)	95%CI*)	OR†)	95%CI†)
Intake of midnight meals:						
seldom	72.7%	83.8%	1.00		1.00	
1-2 times/week	15.9	13.0	1.65	0.63- 4.31	2.22	0.75- 6.51
3-5 times/week	4.6	0.7	6.50	0.56-75.70	8.52	0.62-117.41
Everyday	6.8	2.6	3.04	0.67-13.89	3.86	0.80- 18.63
Trend			1.56	1.01- 2.41	1.67	1.04- 2.67
Intake of vegetables other than yellow or red:						
Seldom	2.3	1.3	1.00		1.00	
1-2 times/week	18.2	9.0	1.22	0.09-16.42	1.27	0.07- 22.60
3-5 times/week	38.6	35.3	0.61	0.05- 6.89	0.76	0.05- 11.57
Everyday	40.9	52.6	0.36	0.03- 4.27	0.42	0.03- 6.85
Trend			0.59	0.38- 0.93	0.61	0.37- 0.99

*): Results with the univariate analysis

†): Results atter weighting of single marital status, number of parities and family history of uterine, ovarian or breast cancer with multivariate analysis.

compared with control subjects. Byers *et al.*[8] found that in only the 30- to 49 -year age group, significantly increased risk of ovarian cancer was seen in women reporting diet low in fiber and vitamin A from vegetables and fruit sources.

Our result of the association of frequent consumption of white vegetables with the reduction of ovarian cancer risk might be somewhat consistent with the previously cited reports. Although we could not confirm the protective effect of yellow or red vegetables, the beta-carotene in them has been shown to play a significantly protective role in the risk of ovarian cancer by case-control studies[9-11]. It may be inferred that fibers and/or vitamins in vegetables would be etiologically important in preventing the initiation or promotion of ovarian cancer cells.

Our finding of a relationship between late meals and ovarian cancer was quite unique, and has not been reported yet elsewhere. Since this finding was still significant after adjustment for single marital status and other variables, we would speculate that midnight meals might have some deleterious effects on hormonal or other biological rhythms; however, much additional evidence must be obtained before this can be discussed seriously.

Frequent consumption of meat has been suggested to significantly increase the risk of ovarian cancer after case-control studies[2,7,9,12], although in this study, the cases and the controls showed no differemce in this regard. The limited sample size of this study may have heen insufficient to detect those previously reported risk factors. This study may also have involved some selection bias and recall bias, because about 30% of the controls did not respond to the survey, and 25% of the cases had been diagnosed more than 2 years before the survey. Nevertheless, this is the first report in Japan which has evaluated the significant and non-significant dietary factors in terms of the risk of ovarian cancer.

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