

Protective Effects of Raw Vegetables and Fruit against Lung Cancer among Smokers and Ex-smokers: A Case-Control Study in the Tokai Area of Japan

Chang-ming Gao,^{1,2} Kazuo Tajima,^{2,3} Tetsuo Kuroishi,² Kaoru Hirose² and Manami Inoue²

¹Jiangsu Institute of Cancer Research, Beiziting 42, Nanjing, China and ²Division of Epidemiology, Aichi Cancer Center Research Institute, 1-1 Kanokoden, Chikusa-ku, Nagoya 464

In a hospital-based case control study, the protecting effects of fruit, raw and green vegetables against lung cancer risk among male smokers were studied in 282 cases and the same number of controls. The current smokers showed a 6.61-fold increased risk of lung cancer. The odds ratio (OR) declined markedly with starting age of smoking habit and increased markedly with number of cigarettes smoked per day. The ex-smokers showed a 3.56-fold increased risk of lung cancer. The ORs gradually decreased with years passed since cessation of smoking. In the single factor analysis, significant protective effects of fruit, raw vegetables, green vegetables, lettuce and cabbage against lung cancer were found. The risk for all lung cancer decreased to 0.45 (95% confidence intervals (CI) 0.30-0.67), 0.64 (95% CI 0.43-0.97) and 0.44 (95% CI 0.26-0.73) with increment of intake frequency of fruit, raw and green vegetables respectively. The OR for lung cancer decreased to 0.41 (95% CI 0.24-0.72) and 0.56 (95% CI 0.32-0.99) with increasing intake frequency of fruit and raw vegetables among current smoking males. Lettuce and cabbage showed protective effects against lung cancer, and the OR for risk of lung cancer decreased to one-half among the high intake frequency group. The risk of lung cancer among current smokers declined markedly with increasing intake of lettuce and cabbage. A similar effect was observed among ex-smokers and non-smokers, but there was no statistical significance. In the multivariate analysis, fruit and raw vegetables showed the strongest protective effects against lung cancer among current smokers ($P=0.01$). Among ex-smokers, the protective effect of fruit is also statistically significant ($P=0.03$). These results suggest that fruit and raw vegetables may play an important role in protecting smokers from lung cancer.

Key words: Lung cancer — Smoking habit — Protective factor — Raw vegetable — Fruit

It has been established that cigarette smoking is a major cause of lung cancer. A survey conducted by the World Health Organization on lung cancer found that 97% of the respondents agreed that at least 80% of all lung cancer cases were caused by tobacco.¹⁾ It was estimated in Japan that 67% of lung cancer cases among men was attributable to cigarette smoking.²⁾ In China, the risks of lung cancer attributable to smoking were 59.7% among males and 25.5% among females.³⁾ Although cessation of smoking is believed to be the best measure for prevention of lung cancer, the prevalence of smoking in the male population aged 20 and over in Japan and China is still high: 61% and 69% respectively.^{4,5)} The risk of lung cancer among smokers will not decrease to the non-smoker's level immediately after cessation of smoking. It is thought that a decrease of cigarette consumption leads to a decrease in lung cancer mortality with a lag time of 24 years in the US.⁶⁾ Protective effects of dietary components against lung cancer have been noted. The effects of leafy green vegetables,⁷⁾ green and yellow vegetables,⁸⁾ dark green and yellow vegetables, cruciferous vegetables,^{9,10)} carrots and toma-

atoes have been examined, with remarkably consistent results. In the present paper, we describe the protective effects against lung cancer due to intake of raw vegetables, green vegetables and fruit in male current and ex-smokers by means of a case-control study.

MATERIALS AND METHODS

Information on life-style has been routinely collected from all the out-patients of the Aichi Cancer Center Hospital, Nagoya, Japan, since 1987. All data were obtained prior to diagnosis, through a self-administered questionnaire under the supervision of an interviewer. In this case-control study, the 282 male cases of lung cancer diagnosed from January 1, 1988 to June 30, 1991 were used. Their ages ranged from 30 to 84 years. A control matched to each case by sex, age (± 1 year) and time of first visit to the hospital (± 30 days), was selected from among out-patients having no evidence of any cancer in this hospital. Patients admitted for diseases of the respiratory system were excluded from the control group. Among the controls, 85.5% had no evidence of any disease. As shown in Table I, 98.6% of lung cancer cases and 96.5% of controls reside in the Tokai area, Japan.

³ To whom all correspondence should be addressed.

The questionnaire included questions on occupation, marriage, family history, cigarette, alcohol and tea consumption and dietary habits. The dietary habits section included questions on intake frequency of raw vegetables and fruit (each as a single item), green vegetable, lettuce, cabbage, carrot, pumpkin, potato, fish and meat, egg, pickles, rice, etc. The cases and controls were classified into 3 categories, current smoker, ex-smoker, and non-smoker according to smoking status. Ex-smokers were defined as those who had smoked in the past and had quit smoking 1 year or more before the date of visiting the hospital.

The odds ratio (OR) and 95% confidence intervals (95%CI) of smoking status by intake frequency of vegetables and fruit were calculated to measure the risk of lung cancer. Logistic multiple regression analysis of the data was performed using the SAS LOGIST procedures.

RESULTS

A total of 282 male pair-matched sets were studied. The mean ages were 61.4 and 61.1 years for cases and controls, with a range from 30 to 83 years. There were 184 current smokers (65.3%) and 85 ex-smokers (30.1%)

Table I. Distribution of Subjects by Age, Area of Residence, Smoking Status and Histologic Types in Cases and Controls

Age groups	Cases		Controls	
	Number	%	Number	%
Age 30-39	13	4.6	12	4.3
40-49	30	10.6	32	11.3
50-59	70	24.8	70	24.8
60-69	95	33.7	98	34.8
70-79	68	24.1	63	22.3
80-83	6	2.1	7	2.5
Mean age (years)	61.4		61.1	
Area of residence				
Tokai area	278	98.6	272	96.5
Aichi	204	72.3	231	81.9
Gifu	50	17.7	20	7.1
Mie	24	8.5	21	7.5
Other areas	4	1.4	10	3.5
Smoking status				
Current smokers	184	65.3	117	41.5
Ex-smokers	85	30.1	109	38.7
Non-smokers	13	4.6	56	19.9
Histologic types				
Squamous cell	80	28.4		
Adenocarcinoma	120	42.6		
Small cell	23	8.2		
Large cell	26	9.2		
Other	8	2.8		
Unknown	25	8.9		
Total	282		282	

in the cases, and there were 117 smokers (41.5%) and 109 ex-smokers (38.7%) in the controls (Table I).

Table II shows the relation of smoking status to lung cancer. The current smokers showed a 6.61-fold increased risk of lung cancer. The OR among current smokers declined markedly with later starting age of the smoking habit and increased markedly with number of cigarettes smoked per day. The ex-smokers showed a 3.56-fold increased risk of lung cancer. The OR gradually decreased with years passed since cessation of smoking.

The overall association between intake frequency of fruit, raw and green vegetables, lettuce, cabbage and lung cancer risk by histologic type is given in Table III. The OR for risk of all lung cancer decreased to 0.45, 0.64 and 0.44 with increment of intake frequency of fruit, raw and green vegetables respectively. Raw lettuce and cabbage usually eaten in Japan showed protective effects against lung cancer, and the OR for risk of lung cancer decreased to 0.51 and 0.39 among the high intake frequency group respectively. The protective effects of raw vegetables and lettuce are statistically significant only for squamous cell carcinoma, the OR for the highest intake category being 0.48 and 0.39. The protective effect from green vegetables is statistically significant only for adenocarcinoma, the OR for the highest intake category being 0.41. Fruit shows protective effects for all histologic types; the decrease of OR is statistically significant for both squamous cell carcinoma and adenocarcinoma. Cabbage showed a significant protective effect against small cell carcinoma.

Table II. Odds Ratio (OR) of Lung Cancer According to Starting Age of Smoking Habit, Number of Cigarettes per Day and Period since Quitting Smoking

Smoking status	Cases	Controls	OR	95%CI
Non-smokers	13	56	1.00	
Current smokers	184	117	6.61 ^{a)}	3.47-12.58
Age started				
-19	52	26	8.62	4.01-18.52
20-29	127	85	6.43	3.32-12.49
30+	2	4	2.15	0.36-13.05
Number of cigarettes/day				
1-19	32	41	3.46	1.57-7.19
20-29	77	44	7.53	3.71-15.30
30+	74	30	10.63	5.08-22.22
Ex-smokers	85	109	3.56 ^{a)}	1.83-6.91
Years since stopped				
1-4	31	26	5.14	2.31-11.40
5-9	21	26	3.48	1.15-8.01
10-14	16	18	3.83	1.55-9.46
15-19	7	9	3.35	1.05-10.66
20+	8	25	1.38	0.51-3.74

a) Adjusted by age.

Table III. Odds Ratio (OR^{a)} of Lung Cancer According to Intake Frequency of Vegetables and Fruit by Histologic Types

Intake frequency	Squamous cell		Adenocarcinoma		Small cell		Large cell		Total ^{b)}	
	Number	OR (95%CI)	Number	OR (95%CI)	Number	OR (95%CI)	Number	OR (95%CI)	Case/Cont.	OR (95%CI)
Fruit										
Almost none and sometimes	40	1.00	55	1.00	10	1.00	11	1.00	135/90	1.00
3-4 times/week	18	0.52 (0.27-0.99)	35	0.72 (0.42-1.23)	5	0.65 (0.22-1.92)	6	0.66 (0.25-1.76)	67/59	0.82 (0.52-1.30)
Every day	22	0.40 (0.22-0.72)	29	0.36 (0.21-0.62)	8	0.63 (0.23-1.72)	9	0.60 (0.25-1.47)	73/126	0.45 (0.30-0.67)
Raw vegetables										
Almost none and sometimes	38	1.00	35	1.00	9	1.00	6	1.00	112/79	1.00
3-4 times/week	17	0.53 (0.28-1.03)	29	0.74 (0.42-1.32)	7	1.01 (0.37-2.74)	9	1.75 (0.63-4.89)	70/72	0.73 (0.46-1.16)
Every day	25	0.48 (0.27-0.87)	46	0.71 (0.42-1.19)	7	0.58 (0.19-1.82)	11	1.31 (0.50-3.44)	95/124	0.64 (0.43-0.97)
Green vegetables										
Almost none and sometimes	43	1.00	73	1.00	15	1.00	16	1.00	164/138	1.00
3-4 times/week	29	1.40 (0.80-2.44)	35	1.00 (0.61-1.65)	5	0.71 (0.27-1.88)	8	1.11 (0.46-2.69)	80/73	1.01 (0.72-1.41)
Every day	7	0.46 (0.21-1.05)	11	0.41 (0.21-0.81)	3	0.58 (0.19-1.81)	3	0.57 (0.19-1.75)	26/56	0.44 (0.26-0.73)
Lettuce										
Almost none	19	1.00	24	1.00	4	1.00	4	1.00	54/32	1.00
≤2 times/week	45	0.47 (0.23-0.96)	68	0.68 (0.36-1.28)	14	0.70 (0.23-2.08)	17	0.74 (0.17-3.31)	158/161	0.57 (0.34-0.94)
≥3 times/week	15	0.39 (0.17-0.90)	28	0.63 (0.31-1.28)	5	0.59 (0.17-2.09)	4	0.55 (0.09-3.28)	62/80	0.51 (0.29-0.90)
Cabbage										
Almost none	7	1.00	9	1.00	4	1.00	1	1.00	22/11	1.00
≤2 times/week	50	0.31 (0.10-0.96)	68	0.35 (0.14-0.87)	13	0.11 (0.03-0.42)	16	0.56 (0.11-2.78)	166/166	0.34 (0.15-0.74)
≥3 times/week	22	0.32 (0.10-1.03)	43	0.48 (0.19-1.21)	6	0.10 (0.03-0.41)	8	0.50 (0.09-2.87)	87/97	0.39 (0.18-0.88)

a) Adjusted by smoking status.

b) Includes cases of unknown histological type.

Some cases and controls were excluded from the analysis because of lack of information.

When the OR values for lung cancer of the five food items among three smoking categories were analyzed, significant protective effects against lung cancer from these food items were observed among current smokers (Table IV). The risk of lung cancer among current smokers declined markedly with increasing intake frequency of the five food items. Daily intake of fruit, raw vegetables and green vegetables decreased the OR for lung cancer to 0.41, 0.56 and 0.48, respectively. Among current smokers taking lettuce and cabbage three times or more per week, the OR decreased to 0.44 and 0.28, respectively. Similar effects were observed among ex-smokers and non-smokers, but no statistical significance in the risk reduction was found.

Table V shows the risk of lung cancer with starting age of smoking and number of cigarettes per day in relation to intake frequency of fruit, raw vegetables, green vegetables, lettuce and cabbage among current smokers. These food items, except cabbage, showed a significant protective effect against lung cancer among the earlier-starting age group and heavy smokers.

The risk of lung cancer with period since quitting cigarette smoking in relation to intake frequency of fruit, raw vegetables, lettuce and cabbage was analyzed among

ex-smokers. Compared to the group with lower intake frequency or almost none, all of the highest intake frequency groups have a lower OR, but the difference among periods since quitting cigarette smoking was not statistically significant (data not shown).

Table VI shows the result of multivariate analysis by the logistic regression model. After adjustment for age, smoking, amount of alcohol, saltiness preference and intake frequency of salted foods, fish and meat, fruit showed the strongest protective effect against lung cancer among all subjects ($P < 0.01$). The protective effect of raw vegetables is also statistically significant ($P < 0.05$). Among current smokers, the protective effects against lung cancer from fruit, raw vegetables and cabbage showed statistical significance, but among ex-smokers, only the protective effect from fruit is statistically significant ($P = 0.03$).

DISCUSSION

The results of epidemiologic studies carried out in different areas of the world have proven that smoking is the main cause of lung cancer, especially among men. In our study, the risk of lung cancer increased with the number

Table IV. Odds Ratio (OR) of Lung Cancer According to Intake Frequency of Fruit, Raw and Green Vegetables, Lettuce and Cabbage by Smoking Status

Frequency	Current smokers		Ex-smokers		Non-smokers	
	Case/Cont.	OR ^{a)} (95%CI)	Case/Cont.	OR ^{b)} (95%CI)	Case/Cont.	OR ^{c)} (95%CI)
Fruit						
Almost none and sometimes	98/42	1.00	33/33	1.00	4/15	1.00
3-4 times/week	40/27	0.66 (0.36-1.23)	24/20	1.25 (0.58-2.67)	3/12	0.94 (0.17-5.02)
Every day	42/46	0.41 (0.24-0.72)	26/51	0.53 (0.27-1.04)	5/29	0.65 (0.15-2.77)
Raw vegetables						
Almost none and sometimes	83/39	1.00	27/27	1.00	2/13	1.00
3-4 times/week	51/29	0.91 (0.50-1.66)	18/29	0.90 (0.38-2.17)	1/14	0.46 (0.04-5.75)
Every day	47/47	0.56 (0.32-0.99)	38/48	0.81 (0.41-1.59)	10/29	2.24 (0.43-11.71)
Green vegetables						
Almost none and sometimes	116/64	1.00	43/53	1.00	5/24	1.00
3-4 times/week	46/30	0.94 (0.53-1.65)	30/27	1.35 (0.70-2.63)	6/16	1.80 (0.67-6.91)
Every day	17/21	0.48 (0.23-1.00)	10/21	0.69 (0.29-1.63)	1/16	0.30 (0.03-2.81)
Lettuce						
Almost none	38/14	1.00	14/11	1.00	2/7	1.00
≤2 times/week	106/69	0.61 (0.31-1.20)	48/65	0.58 (0.24-1.39)	4/27	0.52 (0.08-3.43)
≥3 times/week	36/32	0.44 (0.20-0.95)	20/26	0.60 (0.23-1.61)	6/22	0.95 (0.16-5.85)
Cabbage						
Almost none	12/2	1.00	8/5	1.00	2/4	1.00
≤2 times/week	118/72	0.29 (0.08-0.97)	44/66	0.44 (0.15-1.29)	4/28	0.29 (0.04-2.10)
≥3 times/week	50/40	0.28 (0.08-0.99)	31/31	0.68 (0.22-2.08)	6/26	0.46 (0.07-3.13)

a) Adjusted by smoking index (daily number of cigarettes × smoking years).

b) Adjusted by period since quitting smoking.

c) Not adjusted.

Some cases and controls were excluded from the analysis because of lack of information.

of cigarettes per day, and decreased gradually after cessation of smoking. All of these results suggest the important causative role of cigarette smoking in lung cancer.

Dietary habit is believed to be the second most readily modifiable factor influencing cancer risk, after the smoking habit, since the first report of a protective effect of dietary vitamin A against lung cancer. The risk of lung cancer has been examined in relation to vegetables, fruit and other food groups. Fontham reviewed the relationship between protective dietary factors and lung cancer. High intakes of vegetables and fruit have been associated with relative risk for lung cancer ranging from 0.3 to 0.8.¹¹⁾ The risk of lung cancer increased markedly with declining intake of vegetables, dark green vegetables and dark yellow-orange vegetables.¹⁰⁾ Increased consumption of vegetables and fruit may reduce the risk for lung cancer.^{9, 12-15)} In our study, the relative risk of lung cancer decreased markedly with increment of intake frequency of fruit, raw vegetables, green vegetables, lettuce and cabbage in the single factor analysis. Daily intake of fruit, raw vegetables and green vegetables resulted in OR values of 0.45, 0.64 and 0.44, respectively, and the rela-

tive risk of lung cancer may be decreased to one-half by daily intake of lettuce or cabbage. These results confirm vegetables and fruit to be protective factors against lung cancer.

The pattern of protective effects from vegetables and fruit for lung cancer varies according to histological type and smoking status. Green vegetables show a protective effect only for squamous cell carcinoma (the OR was not statistically significant). Carrots seem to be effective against lung cancer independent of histological type, but only among current smokers in Lombardy, Italy.⁷⁾ In Hawaii, the effect of vegetables against lung cancer was observed for all cell types, but was somewhat stronger for squamous and small cell carcinomas than for adenocarcinoma.¹⁴⁾ In our study, the protective effect of raw vegetables and lettuce was only present for squamous cell carcinoma. The effect of green vegetables was statistically significant for adenocarcinoma. The effect of fruit was seen for both squamous cell carcinoma and adenocarcinoma, while cabbage seemed to be effective for squamous cell carcinoma, small cell carcinoma and adenocarcinoma.

Table V. Age-adjusted Odds Ratio (OR) for Lung Cancer in Subjects with Various Frequencies of Intake of Raw Vegetables and Fruit According to Starting Age of Smoking and Number of Cigarettes in Current Smokers

Intake frequency	Age of smoking started				Number of cigarettes/day			
	10-20		21+		1-19		20+	
	Case/Cont.	OR (95%CI)	Case/Cont.	OR (95%)	Case/Cont.	OR (95%CI)	Case/Cont.	OR (95%CI)
Fruit								
Almost none and sometimes	79/34	1.00	19/8	1.00	19/15	1.00	79/27	1.00
3-4 times/week	35/23	0.64 (0.33-1.25)	5/4	0.53 (0.11-2.49)	4/10	0.25 (0.07-0.88)	37/18	0.70 (0.34-1.44)
Every day	32/36	0.38 (0.20-0.70)	10/10	0.39 (0.12-1.32)	8/16	0.29 (0.10-0.85)	35/29	0.41 (0.21-0.79)
Raw vegetables								
Almost none and sometimes	65/32	1.00	18/7	1.00	12/11	1.00	71/28	1.00
3-4 times/week	44/25	0.86 (0.45-1.63)	7/4	0.68 (0.15-3.07)	7/12	0.50 (0.15-1.67)	44/17	1.03 (0.50-2.10)
Every day	37/36	0.52 (0.28-0.96)	10/11	0.38 (0.12-1.25)	13/18	0.69 (0.24-1.97)	36/29	0.50 (0.26-0.97)
Green vegetables								
Almost none and sometimes	94/54	1.00	23/11	1.00	17/24	1.00	99/39	1.00
3-4 times/week	38/22	1.03 (0.55-1.94)	9/8	0.54 (0.18-1.64)	8/11	1.02 (0.35-2.93)	39/19	0.84 (0.43-1.64)
Every day	15/19	0.45 (0.21-0.95)	3/3	0.79 (0.16-3.93)	6/6	1.18 (0.35-3.99)	12/16	0.29 (0.13-0.66)
Lettuce								
Almost none	31/10	1.00	7/4	1.00 ^{a)}	6/7	1.00	31/7	1.00
≤2 times/week	83/56	0.50 (0.23-1.09)	20/10	1.01 (0.25-4.12)	18/29	0.73 (0.22-2.39)	90/40	0.53 (0.22-1.32)
≥3 times/week	31/27	0.41 (0.17-0.98)	8/6	0.71 (0.12-4.32)	12/9	1.46 (0.39-5.50)	27/23	0.25 (0.09-0.67)
Cabbage								
≤2 times/week	101/62	1.00	29/12	1.00	20/29	1.00	110/44	1.00
≥3 times/week	44/30	0.92 (0.53-1.60)	6/9	0.26 (0.08-0.85)	16/16	1.48 (0.61-3.54)	37/25	0.58 (0.31-1.07)

a) Not adjusted.

Some cases and controls were excluded from the analysis because of lack of information.

Table VI. Analysis of Maximum Likelihood Estimates^{a)} by Logistic Regression According to Smoking Status

	Current smokers ^{b)} (Case/cont. = 168/110)			Ex-smokers ^{c)} (Case/cont. = 77/89)			Non-smokers ^{d)} (Case/cont. = 12/56)			Total ^{e)} (Case/cont. = 265/261)		
	Parameter estimate	Standard error	P value	Parameter estimate	Standard error	P value	Parameter estimate	Standard error	P value	Parameter estimate	Standard error	P value
Fruit ^{f)}	-0.354	0.142	0.01	-0.383	0.179	0.03	-0.274	0.490	0.58	-0.344	0.103	<0.01
Raw vegetables ^{f)}	-0.348	0.140	0.01	-0.121	0.184	0.51	-0.530	0.505	0.29	-0.197	0.101	<0.05
Green vegetables ^{g)}	-0.220	0.152	0.15	-0.089	0.172	0.61	-0.173	0.436	0.69	-0.167	0.105	0.11
Lettuce ^{g)}	-0.167	0.119	0.16	-0.116	0.147	0.43	0.344	0.389	0.38	-0.111	0.086	0.20
Cabbage ^{g)}	-0.309	0.153	0.04	0.092	0.168	0.59	-0.383	0.457	0.40	-0.126	0.104	0.22

a) Fruit and vegetables (including other vegetable variables) were not adjusted simultaneously because they are strongly related to each other ($P=0.0001$).

b) Adjusted by age, starting age of smoking, smoking index, amount of alcohol, saltiness preference and intake frequency of salted foods, fish and meat.

c) Adjusted by age, smoking index, years since quitting smoking, amount of alcohol, saltiness preference and intake frequency of salted foods, fish and meat.

d) Adjusted by age, amount of alcohol, saltiness preference and intake frequency of salted foods, fish and meat.

e) Adjusted by age, smoking status, smoking index, amount of alcohol, saltiness preference and intake frequency of salted foods, fish and meat.

f) Scores: 1, almost none; 2, sometimes; 3, 3-4 times/week; 4, every day.

g) Scores: 1, almost none; 2, 1-2 times/month; 3, 1-2 times/week; 4, 3-4 times/week; 5, every day.

The relationship between cigarette smoking and vegetables and fruit intake has been examined. There is an inverse association with vegetable intake among currently smoking men in New Jersey and in Hawaii, but no statistical significance among ex-smokers and non-smokers.^{10, 14)} In those smoking, drinking alcohol and eating meat daily, the daily consumption of green-yellow vegetables was found to lower the risk of lung cancer in Hirayama's large cohort study in Japan.⁸⁾ In our study, the relationship between smoking habits and intake frequency of fruit, raw vegetables, green vegetables, lettuce and cabbage was examined closely. In the single factor analysis, the results showed that fruit, raw vegetables, lettuce and cabbage have a marked effect for the prevention of lung cancer, with a clear dose-response relationship among current smokers, but in ex-smokers and non-smokers these effects did not show statistical significance. In the multivariate analysis, fruit showed the strongest protective effect among current smokers, ex-smokers and all subjects. The protective effects of raw vegetables and cabbage also showed statistical significance among current smokers.

A significant protective effect of vitamin C against lung cancer has been found.¹⁶⁾ Animal studies have provided convincing evidence that retinol and synthetic retinoids are protective against epithelial tumors including lung cancer. The promotion or progression of carcinogenesis might be blocked by retinoids when administered during the latent period after initiation. Serum beta-carotene showed a strong inverse association with the risk of lung cancer.¹⁷⁾ Lung cancer patients had significantly lower serum levels of carotenoids, and low levels of beta-carotene in serum or plasma are consistently associated with the subsequent development of lung cancer.^{18, 19)} Fruit and vegetables are common sources of many candidate protective substances, including vitamin C, beta-carotene and other carotenoids with and without vitamin A activity. Carotenoids are strong antioxidants and as such are capable of quenching singlet oxygen and blocking the carcinogenic effects of free radicals.²⁰⁾ It was shown by Tanabe *et al.* that the serum beta-carotene level was significantly lower in smokers than in non-smokers (ex-smokers were included), and it was higher in the group with a greater intake of vitamin A of vegetable

origin than in the group with a smaller intake.²¹⁾ Large quantities of peroxide and superoxide are present in cigarette smoke and the smoking habit is associated with exposure to activated oxygen. In our study, the protective effects against lung cancer of raw vegetables and fruit have no significance among non-smokers. There are three possible explanation for these results. The first is that the non-smokers may have a higher serum carotenoids level or lower activated oxygen level than smokers. The second is that prevention by raw vegetables and fruit might involve later stages of lung carcinogenesis. The third is that the failure to note a protective effect of intake of raw vegetable and fruit among non-smokers was due to the smaller number of non-smoking cases.

This study contains several methodological problems, as do other case-control studies. For example, the controls were selected from the outpatients of a cancer hospital and respiratory diseases were excluded, so the distribution of smoking status among controls may not represent that in the general population. The rate of ex-smokers was relatively higher but that of current smokers was lower in this control group compared to those in the general population. This may be due to a greater health consciousness among patients visiting a cancer hospital. But, because linear trends of risk reduction of lung cancer with higher intake of raw vegetables and fruit were observed in this study, it seems possible that raw vegetables and fruit do reduce the risk of lung cancer in smokers. To evaluate these issues, a further study using a broader sample and more precise analysis will be necessary.

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