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Tobacco, Alcohol and Dietary Factors Associated with the Risk of Oral Cancer among Japanese

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The mortality rate among Japanese men due to oral cancer is increasing, but risk factors among Japanese other than smoking and drinking have not been examined. To investigate the dietary factors involved in oral cancer, we conducted a hospital-based case-referent study in Aichi, Japan. Cases comprised 189 men and 77 women aged 20–79 years with one of the following cancers: tongue, mouth, oropharynx and hypopharynx. The reference group comprised 9,858 male and 26,669 female outpatients without cancer. Smoking and drinking were highly associated with an increased risk of oral cancer. Japanese sake showed a lower odds ratio (OR) than beer or hard liquor (OR=3.6, 4.5 and 4.8, respectively). In the cross analysis between smoking and drinking, smoking combined with drinking increased the risk of oral cancer to three times that of smoking only (OR=6.2 vs. 2.2). Frequent intake of raw vegetables (OR=0.5) and fruit (OR=0.5) were inversely associated with the risk of oral cancer after adjustment for age, sex, smoking, drinking and year of visit. Western-style breakfast and salty food preference decreased the risk of oral cancer, and salty food preference was still statistically significant by multivariate analysis (OR=0.7). In conclusion, smoking cessation, drinking control and frequent intake of raw vegetables and fruit among Japanese are likely to be effective preventive measures against oral cancer.

Key words: Oral cancer — Case-referent study — Raw vegetables — Fruit — Japanese

Since 1950, the mortality rate in Japanese men due to oral cancer has increased.[1] However, the age-adjusted mortality rate in Japanese men due to oral cancer is less than half of that of white US men, whose mortality rate decreased during 1955 to 1985.[2] In contrast, Japanese women did not show an increased trend of oral cancer mortality and its age-adjusted rate during the same period was much lower among Japanese women than white US women or Japanese men.

Smoking and alcohol consumption are the major risk factors in oral cancer.[3–5] Therefore, the increased cigarette smoking and alcohol consumption in Japanese men and decreased smoking in white US men may mainly have contributed to the changed trend in oral cancer mortality during 1955 to 1985.[2] Some dietary factors and oral cavity factors have been reported to be associated with the risk of oral cancer.[6,7] As preventive measures against oral cancer, therefore, dietary factors in addition to smoking cessation and drinking control may be important. The Japanese dietary habit is different from that of Westerners, but there has been no study investigating the influence of dietary factors on oral cancer among Japanese. To investigate this point, we conducted a hospital-based case-referent study in Aichi, Japan, using all eligible non-cancer outpatients of Aichi Cancer Center Hospital (ACCH) as the reference group.

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MATERIALS AND METHODS

Since 1988, a self-administered questionnaire has been completed by all first-visit outpatients to ACCH in Aichi prefecture, Japan, to get information on lifestyle and medical history before the onset of symptoms. Details of the questionnaire and data collection procedures have been described elsewhere.[8,9] An expert interviewer checks all written responses at the time of collection. Included are questions on demography, past history, family history, smoking, drinking habits, general health status, reproductive status, and beverage and food intake before symptoms appeared.

Between 1988 and 1993, 43,775 (91.4%) of all first-visit outpatients (n=47,895) responded to the questionnaire. The remaining respondents were excluded because of: absence of the interviewer (n=1,568, 3.3%); being under 18 years of age (n=530, 1.1%); failure to collect the questionnaire (n=460, 1.1%); refusal to participate (n=17, 0.04%); various other reasons (n=1,561, 3.3%). Among all outpatients, 6,170 (14.1%) were diag-

nosed as having cancer and registered with the hospital cancer-registry system of ACCH; malignant neoplasms were ruled out in 37,605 (85.9%) outpatients.

The cases in the present study were 189 men and 77 women who visited ACCH from 1988 to 1993, and within one year of responding to the questionnaire (at which time they were between 20–79 years old) were histologically diagnosed as having primary oral cancer as follows: tongue (ICD-9, 141), mouth (143–5), oropharynx (146) and hypopharynx (148).

The reference group was selected from all first-visit outpatients who were between 20–79 years old and who had been confirmed to be cancer-free by diagnostic procedures at ACCH between 1988 and 1993. As the Japanese medical system for outpatients is quite different from that of other countries, and most hospitals, including ACCH, permit visits to outpatient departments without doctor's referrals, we could collect much information on non-cancer respondents from ACCH outpatients. The actual number of outpatients with doctor's referrals was 4,476 (11.9%) of all non-cancer outpatients. To assess the proportional distribution of clinical diagnoses among non-cancer outpatients, we randomly sampled 10% of those outpatients (n=2,997) between 1988 and 1992 and confirmed their final diagnosis from medical records[10] (Table I). Forty-four percent were found to have shown no abnormal findings in examinations; 13% had benign tumors or non-neoplastic polyps; and the other 35% were confirmed to have benign and nonspecific diseases. Tobacco-related diseases such as chronic bronchitis and emphysema amounted to less than 1%. After excluding 467 outpatients with a history of cancer, 9,858 men and 26,669 women were eligible for the reference group.

The proportional distribution of places where cases and referents were living was 74.8% and 84.5% in Aichi prefecture, and 33.8% and 42.8% in Nagoya city, respectively.

Table I. Proportional Distribution of Diagnoses among Non-cancer Outpatients[a] in ACCH (1988–1992)

Diagnosis	(%)
Disease-free	44.3
Benign tumor, non-neoplastic polyp	13.1
Cystic diseases	3.4
Other diseases	
Mastitis of breast	7.5
Upper gastro-intestinal tract	4.1
Reproductive system	4.1
Hepatobiliary system and pancreas	1.5
Respiratory system	1.2
Miscellaneous	20.8
Total	100.0

a) Randomly selected 10% of non-cancer outpatients (n=2997/31782).

Smokers were defined as being current or ex-smokers who had smoked cigarettes for more than one year. Smoking factors were analyzed according to smoking duration, age at which smoking started, years since quitting smoking, and cigarette consumption before having symptoms. Alcohol intake of each type of beverage (Japanese sake, beer and hard liquor) was determined as the average number of drinks per day, which was then converted into a Japanese sake (rice wine) equivalent. One drink equates to one "go" (180 ml) of Japanese sake which contains 27 g of ethanol, one regular bottle (633 ml) of beer or two shots (57 ml) of hard liquor. "Shochu" (low-grade distilled spirit) which contains 25% ethanol was included as hard liquor and one drink was rated as equivalent to 108 ml of "Shochu." Wine was not included in the present questionnaire, because few Japanese drink it regularly. As some respondents drank several types of alcoholic beverages according to the season, the types of alcohol beverages were analyzed if respondents drank the same type both in summer and in winter. When odds ratios (ORs) were adjusted for alcohol drinking, drinkers were defined as those who drank more than 2 drinks/day and more than 4 times/week (regular drinker).

Dietary items were divided into 4 or 5 groups according to respondent intake frequency. These groups were further divided into tercile subgroups, each tercile subgroup comprising approximately one-third of referents. The intake frequencies of pickles, meat and green-yellow vegetables were divided into tercile subgroups according to respondent intake frequency by adding related food items as follows; pickles: Chinese cabbage and fresh vegetables, meat: beef, pork and chicken, green-yellow vegetables: green vegetables, carrot and pumpkin. As the Japanese have two styles of breakfast (Japanese style: rice and miso soup, Western style: bread and coffee), we asked respondents what kind of breakfast they used to take before having symptoms. To get information on general dietary habits, respondents were asked to categorize their preference for salty and greasy foods as follows; 1) like, 2) somewhat like, 3) somewhat dislike and 4) dislike.

For data analysis, ORs and 95% confidence interval (CI) of all items for cases and referents were calculated using unconditional logistic regression models, adjusted for age, sex and year of visit (continuous).[11] The *P*-value was computed using the 2-tailed value of the χ^2 test. To control the effect of confounding factors, multivariate logistic regression models, adjusted for age, sex and year of visit, were used for the analysis among the items of smoking, drinking, type of breakfast, intake of raw vegetables, fruit and miso soup, and the preference for salty

Table II. Distribution of Oral Cancer Cases and Referents by Age, Sex and Site of Cancer, ACCH (1988–1993)

	Number (%) of			
	Cases		Referents	
	Men	Women	Men	Women
Age				
20–29	7 (3.7)	4 (5.2)	757 (7.7)	2545 (9.5)
30–39	11 (5.8)	7 (9.1)	1273 (12.9)	5226 (19.6)
40–49	38 (20.1)	14 (18.2)	2639 (26.8)	9601 (36.0)
50–59	50 (26.5)	14 (18.2)	2561 (26.0)	5595 (21.0)
60–69	57 (30.1)	21 (27.3)	1929 (19.6)	2858 (10.7)
70–79	26 (13.8)	17 (22.1)	699 (7.1)	844 (3.2)
Total	189 (100)	77 (100)	9858 (100)	26669 (100)
Smoking				
never	11 (5.8)	60 (77.9)	2152 (21.8)	22306 (83.6)
ex-	57 (30.2)	10 (13.0)	3015 (30.6)	1085 (4.1)
current	121 (64.0)	7 (9.1)	4684 (47.5)	3252 (12.2)
unknown	0 (0.0)	0 (0.0)	7 (0.1)	26 (0.1)
Drinking				
never & <4 times/week	59 (31.2)	68 (88.3)	4680 (47.5)	24160 (90.6)
≥4 times/week	129 (68.3)	9 (11.7)	5145 (52.2)	2485 (9.3)
unknown	1 (0.5)	0 (0.0)	33 (0.3)	24 (0.1)
Site (ICD9)				
Tongue (141)	93 (49.2)	53 (68.8)		
Mouth (143–5)	44 (23.3)	13 (16.9)		
Oropharynx (146)	25 (13.2)	10 (13.0)		
Hypopharynx (148)	27 (14.3)	1 (1.3)		

food. The LOGISTIC procedure from SAS was used for calculation.[12]

All eligible referents were used for analysis without matching, because our previous study using as subjects the outpatients of ACCH between 1988–1990 showed that analysis based on a large number of referents gave a steadier estimate than matched analysis.[13]

RESULTS

Most cases were more than 40 years old and the age distribution of referents was shifted slightly towards younger-aged groups as compared with cases. The proportional percentages of cases and referents aged more than 40 years were 90.5% and 79.4% in men, and 85.7% and 70.9% in women, respectively. The number of male cases was 2.5 times higher than that of female cases. The prevalence of current smokers and regular drinkers among cases was higher than that among referents in men, but there was no difference in these prevalences between cases and referents in women. The proportion of tongue cancer compared with other cancers was highest among both men and women, being more common among women (Table II).

Table III. Comparison of Oral Cancer Cases to Referents by Smoking History

Smoking history	No. of cases/referents	OR[a)]	95% CI
Never smoked	71/24458	1.0	
No. of cigarettes/day			
1–19	56/5048	2.4**	1.5–3.6
20–39	108/5529	2.8**	1.8–4.5
40+	27/1319	3.5**	1.8–7.0
Years of cigarette smoking			
1–19	31/5148	2.3**	1.4–3.8
20–29	93/5238	2.5**	1.6–3.9
40+	62/1354	2.9**	1.6–5.2
Age smoking started			
–19	49/3134	4.8**	2.6–8.6
20–24	121/6492	2.7**	1.7–4.2
25+	19/2246	1.5	0.9–2.7
Years since quit smoking			
0 (never quit)	128/7936	2.5**	1.7–3.7
1–4	19/961	4.1**	2.1–7.9
5–14	16/1624	1.6	0.8–3.2
15+	13/950	1.7	0.8–3.7

a) All ORs adjusted for age, sex, year of visit and alcohol consumption. χ^2 test for case-referent difference; * $P<0.05$, ** $P<0.01$.

Table III shows the comparison of oral cancer cases to referents by smoking history, adjusted for age, sex, year of visit and alcohol consumption. In "smokers" cases, ORs were elevated according to the number of cigarettes per day, years of cigarette smoking, and age begun. "Ex-smokers" cases who had quit smoking within 1–4 years before the interview showed a higher OR than current smokers, but the ORs decreased among ex-smokers who had stopped smoking more than 5 years before interview.

The OR of habitual drinking ($\geq$4 times/week and $\geq$2 drinks/day) in any category of alcohol beverage was highest for hard liquor (OR=4.8). Alcohol abstainers did not show decreased ORs of oral cancer (Table IV). When the mean alcohol consumption among regular drinkers was compared by type of alcoholic beverage, the hard liquor drinkers tended to drink more alcohol than other groups; Japanese sake: 3.1 drinks/day among cases vs. 2.6 among referents; beer: 2.9 vs. 2.6; hard liquor: 4.2 vs. 3.0, respectively.

The joint effects of smoking and alcohol drinking are shown in Table V. Smokers with a drinking habit showed the highest OR (OR=6.2), adjusted for age, sex and year of visit. The OR among non-drinking smokers was 2.2. There was no case of regular drinking without smoking.

The mean tobacco consumption was higher in male smokers than in female smokers; 23.9 and 12.9 cigarettes/day among cases, and 23.5 and 13.3 among referents, respectively. However, the mean alcohol consumptions were apparently not different between male and female regular drinkers; i.e., 3.2 and 4.0 drinks/day among cases, and 3.1 and 3.5 among referents, respectively (data not shown).

Table IV. Comparison of Oral Cancer Cases to Controls by Alcohol Consumption

Alcohol consumption	No. of cases/referents	OR[a)]	95% CI
Any kind of alcoholic beverage			
Almost never drink	97/21800	1.0	
<4 times/week	30/7008	0.9	0.6–1.4
≥4 times/week, <2 drinks/day	63/5054	1.4	0.95–2.0
≥4 times/week, ≥2 drinks/day	75/2531	2.9**	1.9–4.2
Japanese sake (≥4 times/week)			
<2 drinks/day	7/302	1.3	0.6–3.0
≥2 drinks/day	24/437	3.6**	2.1–6.1
Beer (≥4 times/week)			
<2 drinks/day	18/2310	1.3	0.8–2.3
≥2 drinks/day	14/442	4.5**	2.4–8.6
Hard liquor (≥4 times/week)			
<2 drinks/day	4/154	2.7	0.9–7.6
≥2 drinks/day	12/243	4.8**	2.4–9.3
Years since quit drinking			
0 (never quit)	138/13811	1.2	0.9–1.6
0–4	9/320	2.4*	1.1–5.1
5–14	4/180	1.7	0.6–4.8
15+	4/62	3.4*	1.2–9.9

a) All ORs adjusted for age, sex, year of visit and smoking. χ^2 test for case-referent difference; * $P<0.05$, ** $P<0.01$.

Table V. Comparison of Oral Cancer Cases to Controls by Smoking and Drinking

	Number of cases/referents	OR[a)]	95% CI
Smoking[b)] (−), drinking[c)] (−)	71/24070	1.0	
Smoking (−), drinking (+)	0/333	—	—
Smoking (+), drinking (−)	119/9770	2.2**	1.5–3.2
Smoking (+), drinking (+)	75/2197	6.2**	3.6–10.7

a) All ORs adjusted for age, sex and year of visit. χ^2 test for case-referent difference; ** $P<0.01$.
b) Smoking; current or ex-smoker vs. never smoked.
c) Drinking; ≥4 times/week & ≥2 drinks/day vs. less.

Table VI. Comparison of Oral Cancer Cases to Referents According to Intake Frequency by Selected Dietary Items

Dietary items	Number of cases/referents			ORs[a] [95% CI]		
	Intake frequency			Intake frequency		
	1	2	3	1	2	3
Japanese-style food						
Miso soup	73/14165	151/18600	41/3719	1.0	1.3 [0.98–1.7]	1.3 [0.9–2.0]
Tofu	37/5608	183/25103	46/5735	1.0	1.2 [0.8–1.7]	1.0 [0.7–1.6]
Pickles	101/13808	75/11692	89/10893	1.0	0.8 [0.6–1.1]	0.8 [0.6–1.1]
Fish	39/7045	200/26799	27/2585	1.0	1.2 [0.8–1.7]	1.1 [0.6–1.8]
Western-style food						
Meat	120/12601	108/16738	35/6957	1.0	1.0 [0.8–1.3]	0.9 [0.6–1.3]
Milk	157/20515	78/12089	31/3815	1.0	0.9 [0.7–1.2]	1.2 [0.8–1.8]
Egg	21/2835	142/20577	102/13064	1.0	1.2 [0.7–1.9]	1.4 [0.8–2.2]
Western-style breakfast	171/16479	31/6912	50/10999	1.0	0.7 [0.5–1.1]	0.6** [0.4–0.8]
Vegetables and fruit						
Green-yellow vegetables	121/12758	81/12317	61/11214	1.0	1.0 [0.7–1.3]	1.0 [0.7–1.3]
Raw vegetables	120/10007	66/12375	78/14039	1.0	0.6** [0.4–0.8]	0.5** [0.4–0.7]
fruit	124/10844	60/10335	82/15247	1.0	0.7* [0.5–0.99]	0.5** [0.4–0.7]
Beverages						
Green tea[b]	31/4370	67/10330	51/7007	1.0	0.8 [0.5–1.3]	0.8 [0.5–1.3]
Coffee	39/4724	24/4123	87/12905	1.0	0.8 [0.5–1.4]	0.9 [0.6–1.4]

a) All ORs adjusted for age, sex, smoking, drinking and year of visit. χ^2 test for case-referent difference; * $P<0.05$, ** $P<0.01$.
b) Subjects from 1990 to 1993.

Table VII. Comparison of Oral Cancer Cases to Referents According to Salty Food or Greasy Food Preference

Dietary preference	Number of cases/referents			ORs[a] [95% CI]		
	Preference[b]			Preference[b]		
	1	2	3	1	2	3
Salty food	91/12624	100/15596	71/8022	1.0	0.7* [0.6–0.99]	0.8 [0.6–1.09]
Greasy food	99/17224	113/14278	49/4684	1.0	1.3 [0.96–1.7]	1.3 [0.9–1.8]

a) All ORs adjusted for age, sex, smoking, drinking and year of visit. χ^2 test for case-referent difference; * $P<0.05$.
b) Preference; 1: dislike or somewhat dislike, 2: somewhat like, 3: like.

In Table VI, dietary factors were analyzed by tercile intake frequencies, adjusted for age, sex, smoking, alcohol consumption and year of visit. Raw vegetable intake (ORs=0.6, 0.5) and fruit intake (ORs=0.7, 0.5) were inversely associated with the risk of oral cancer, and these ORs were statistically significant in both subgroups. The frequent intake of miso soup and pickles showed an increased OR of 1.3 and a decreased OR of 0.8, respectively. The decreased OR of frequent green tea consumption was not significant. The subjects who preferred salty food tended to be associated with an inverse risk of oral cancer, and the OR (0.7) of the second subgroup was statistically significant (Table VII). When a validation test on the correlation between the preference and intake frequencies of salty foods was attempted, the Mantel-Haenszel χ^2 test showed a statistically significant correlation between salty food preference and increasing intake frequencies of salty fish ($P<0.01$, $P<0.01$) and Hakusai pickles ($P=0.01$, $P<0.01$) among cases and referents, respectively.

When multivariate logistic regression models, adjusted for age, sex and year of visit, were applied to men and women, smoking and drinking were still involved in an increased risk of oral cancer in men, and men and women. Raw vegetable intake in men, and fruit and salty food preference in women were associated with a reduction in risk of oral cancer (Table VIII).

DISCUSSION

Methodological issues There are several biases in a case-control study. Because we used non-cancer out-

Table VIII. Multivariate Analysis among Men and Women by Smoking, Drinking, Type of Breakfast, Intake of Raw Vegetables, Fruit and Miso Soup, and Salty Food Preference

	Men		Women		Men & Women	
	ORs[a)]	[95% CI]	ORs[a)]	[95% CI]	ORs[b)]	[95% CI]
Smoking[c)]	3.4**	[1.8–6.4]	1.7	[0.9–3.2]	2.3**	[1.6–3.4]
Drinking[d)]	1.9**	[1.4–2.7]	1.0	[0.1–7.6]	1.9**	[1.4–2.6]
Raw vegetables[e)]	0.5**	[0.4–0.7]	0.8	[0.5–1.3]	0.6**	[0.4–0.8]
Fruit[f)]	1.0	[0.7–1.4]	0.5*	[0.3–0.9]	0.8	[0.6–1.1]
Western-style breakfast[g)]	0.6*	[0.4–0.9]	1.0	[0.6–1.7]	0.7	[0.5–1.0]
Miso soup[h)]	1.1	[0.8–1.7]	1.6	[0.9–2.8]	1.3	[0.9–1.7]
Salty food[i)]	0.7	[0.5–1.03]	0.6*	[0.4–0.98]	0.7*	[0.5–0.9]

a) ORs adjusted for age and year of visit.
b) ORs adjusted for age, sex and year of visit.
c) Smoking; current or ex-smokers vs. never smoked.
d) Drinking; $\geq$4 times/week & $\geq$2 drinks/day vs. less.
e, f) Raw vegetables and fruit intake; $\geq$3 times/week vs. less.
g) Type of breakfast; Western style vs. Japanese or mixed style.
h) Miso soup intake; every day vs. less.
i) Salty food preference; like or somewhat like vs. dislike or somewhat dislike.
j) χ^2 test for case-referent difference; * $P<0.05$, ** $P<0.01$.

patients as the reference group in a hospital-based study, selection bias should be considered. ACCH is a cancer hospital, but is open to anyone, with or without doctor's referral. Therefore, malignant neoplasms were ruled out in 86% of all outpatients, and 44% of outpatients among all non-cancer patients were diagnosed as being disease-free. Moreover, tobacco-related diseases such as chronic bronchitis and emphysema were less frequent (<1%) among randomly selected referents. Cases tended to come from more distant places than referents. However, the difference in the distribution of places of residence between cases and referents did not significantly influence the results. Recent prevalence rates of never-smokers, ex-smokers and current-smokers among the general population are 21%, 21% and 58% in men, and 81%, 5% and 14% in women, respectively ("A Report of Awareness Survey on Health Promotion in 1990," Japan Health Promotion and Fitness Foundation). The prevalence rate of never-smokers among the referents is not different from that of the general Japanese population, and ex-smokers are more prevalent among the referents than the general population in men, but not in women. As these rates are compared without age adjustment and current smokers are more prevalent among the general younger population, the rate of ex-smokers in the referents including more aged people may be slightly overestimated. As the proportion of male current and ex-smokers among referents was very similar to that among the male general population (78% vs. 79%) and we analyzed smoking factors among current smokers plus ex-smokers with adjustment for age, the overestimation of the ORs may be reduced. As judged from these facts, the character of the referents in the present study is closer to that of the general population than that of tobacco-related cancer. Furthermore, we used all eligible non-cancer outpatients for referents. A large number of referents reduces the selection bias and gives a steadier estimate than matched analysis.[13] The information bias is small in the present study, because subjects answered the questionnaire before diagnosis was made.

Tobacco and alcohol It is known that tobacco smoking and alcohol drinking are involved in the risk of oral cancer.[3–5] Our results showing the increased risk associated with smoking and drinking among Japanese men are consistent with those of previous studies.[3–5] The increased risk among ex-smokers who quit 1–4 years before the present interview may be explained by the result-bias that more cases had quit smoking within a period of several years before the diagnosis because of symptoms. Female smokers in the present study did not show an apparent increased risk in multivariate analysis, which may, in part, stem from the fact that female smokers consumed fewer cigarettes than male smokers.

In the present study, increased risk of oral cancer was found in regular drinkers of all alcoholic beverages, including Japanese sake, where the OR was lower than those for beer and hard liquor. Wine has also been shown to have a smaller OR than beer and hard liquor in another study.[14] The OR of hard liquor was highest, because hard liquor drinkers drank proportionately more alcohol and also hard liquor is more likely to damage the oral cavity owing to its higher concentration of alcohol. Furthermore, nutritional deficiencies among alcoholic patients play a role in cancer etiology.[15] It has been sug-

gested that ingredients in alcoholic beverages other than ethanol might be involved, for example, nitrosamines and polycyclic hydrocarbons in beer and whiskey.[5, 16] The small difference in the ORs between hard liquor and other spirits in the present study may stem from the fact that the Japanese customarily dilute the liquor more than Westerners do, when they drink hard liquor.

The joint effect of smoking and drinking increases the risk of oral cancer, to triple the risk of smoking only, as shown in previous studies.[4, 5, 17, 18]

Diet Raw vegetables and fruit have been found to have an inverse association with the risk of oral cancer.[6, 7, 19] Smokers and alcohol drinkers tend to consume raw vegetables and fruit less frequently,[20] and may display the nutritional deficiency often associated with alcoholism.[15] However, these inverse associations were still statistically significant after adjustment for smoking and drinking. These protective effects among smokers were also found in our study on lung cancer.[8] Glutathione, fiber and some antioxidants such as beta-carotene, vitamin C, vitamin E and retinol in raw vegetables and fruit might have a protective effect against the development of oral cancer.[5, 7, 21]

Consumption of green-yellow vegetables, including cooked ones, did not provide similar protection. This finding has also been noted in a US study, which suggests an influence of other constituents in fruit and/or a nutrient-diminishing effect in the cooking of vegetables.[6] From the results of multivariate analysis, raw vegetable intake played an important protective role against oral cancer among men, and fruit intake did so among women. It is possible that fruit intake is effective in reducing oral cancer risk, other than from smoking and drinking, in women.

Western-style breakfast seems to be associated with a decreased risk of oral cancer. The referents who frequently consumed western-style breakfast ate raw vegetables and fruit more frequently than those who took Japanese-style breakfast (data not shown). However, the tendency of a decreased OR of western-style breakfast was still shown by multivariate analysis adjusted for raw vegetable and fruit intake. Western-style breakfast consumers may, however, be expected to enjoy other protective factors through their lifestyle, in contrast to Japanese breakfast consumers.

Frequent miso soup intake showed a tendency to be associated with an increasing risk, especially among women. Miso soup might damage the oral mucosa if taken hot.

Cases who preferred salty food showed an inverse association with the risk of oral cancer in the present study. This decreasing risk might be influenced by the result that cases who had suffered from oral cancer changed their consumption preference because of pain or damage to the taste buds, although we requested that respondents let us know their preferences before symptoms had appeared. The association of salty food with decreasing risk of oral cancer should be evaluated more carefully, and more detailed information is needed.

Other factors may be involved in the risk of oral cancer among most women, because 78% of female cases did not smoke or drink. Poor oral hygiene and dental health have been found to be associated with an increasing risk of oral cancer.[22, 23] Furthermore, the use of mouthwash with a high alcohol content has been reported to be associated with increased risk of oral cancer in the US, although mouthwash use is not customary in Japan.[24] Recently, the relationship between oral cancer and infection with human papillomaviruses, herpes simplex virus and Epstein-Barr virus has been studied.[25, 26] To clarify these risk factors, another study including detailed information on oral cavity condition and viral investigation, especially focused on non-smoking women, is needed.

In conclusion, our results showed that, in Japan, frequent raw vegetable and fruit intake was associated with a decreased risk of oral cancer. These dietary habits should be encouraged as preventive measures against oral cancer, in addition to smoking cessation and drinking control. Japanese food did not show any reducing effect on risk of oral cancer. Cases who preferred salty food were associated with a decreased risk of oral cancer, but this association should be evaluated more carefully.

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