Relationship Between Serum Carotenoid Levels and Cancer Death Rates in the Residents, Living in a Rural Area of Hokkaido, Japan

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The relationship between serum carotenoid levels and cancer death in rural Japanese residents, aged more than 39 years, was examined epidemiologically. The follow-up subjects participated in the comprehensive health examinations, every August from 1986 to 1989, were 929 males and 1424 females, living in a rural area of Hokkaido, Japan. During 2-8 years to December 1994, the ninety-eight deaths were observed among the cohort; that is, deaths from all causes were 67 males and 31 females, and cancer deaths were 34 males and 10 females. Serum samples at fasting were collected at the entry of the cohort and serum levels of β-carotene, α-carotene and lycopene were measured by the HPLC method. The relation between the mortality rates and serum carotenoid levels was estimated statistically using the Cox’s proportional hazard model. The results were as follows; the hazard ratio with the overall on high serum β-carotene levels to those of lower was 0.46 (95% C.I.:0.27-0.78) for all causes and 0.33 (95% C.I.:0.14-0.75) for cancer deaths. This result suggested that high levels of serum β-carotene may play some roles on preventing cancer death.

Recent epidemiologic studies were demonstrated that the dietary vitamin A and/or β-carotene intake from foods was considered to be an important factor determining human cancer risk. In Japan, Hirayama reported that high intake of green yellow vegetables was significantly associated with lower cancer mortality rates of the lung, esophagus, and stomach among the large-scale cohort consisting of about two hundred seventy thousand residents after during 15 years observation. He expected that high dietary β-carotene consumption might reduce risk of human cancer. Peto et al have also summarized many studies that some human cancer risks were inversely associated with dietary β-carotene consumption and also with high blood β-carotene levels, as serum β-carotene levels reflected with dietary β-carotene consumption. Since then, there were many epidemiological studies which have shown similar results such high dietary β-carotene consumption from foods was a protective factor for certain types of cancer.

Recently, serum β-carotene concentration could separately be measured and other carotenoids such as α-carotene, lycopene, xanthophylls and others were also quantified respectively. And the serum levels of β-carotene by new measure have shown the similar results in relation to cancer incidence and/or mortality rates, especially for lung cancer in epidemiological studies. It is reported that the intervention trials on β-carotene administration for the male smokers in Finland or for the industrial workers exposed to asbestos with smoking habits showed a slightly increase tendency in the incidence of lung cancer during 4-8 years observation. That was a controversial result as not expected. Among non-smoking groups, however, β-carotene might have shown protective effects on cancer.

We have been following up a cohort population for cancer study. The participants were measured serum levels of β-carotene separating from α-carotene, lycopene and other carotenoids. Therefore, we try to examine whether higher serum levels of β-carotene, α-carotene or lycopene are related to lower death rates of cancer or not, although a number of the subjects are not large.

SUBJECTS AND METHODS

Comprehensive Health Examination Program (CHEP) for...
the inhabitants, aged more than 39 years, has been conducted in Y-town - a rural area of southern Hokkaido, Japan, every August since 1986 by the town office in collaboration with the staffs of Nagoya University School of Medicine, Fujita Health University Schools of Medicine and Health Sciences, Aichi Medical University, Kyoto Prefectural University of Medicine, and Aichi Cancer Center. This health program was started in 1982 and intensified in 1986. A total number of the participants in this CHEP during 1986-1989 was 3639 (1404 males and 2235 females) and all the subjects except two cases were measured their serum carotenoid levels. Among them, 2353 subjects aged from 39y to 83y (929 males: 66.2% and 1424 females: 63.7%), were actual numbers excluded the participants who were attended the CHEP more than two times. All 2353 subjects except 5 deaths (3 males and 2 females) within 12 months after the measurement of serum carotenoids could be followed up until the end of 1994.

The CHEP included physical examinations such as height, weight, visual forces, hearing ability, blood pressures, ECG, endoscopy, chest X-ray, abdominal survey by ultrasound diagnostic method and prostate screening, orthopaeic examination and neurologic check-ups, urine tests, and blood tests. Screening for stomach cancer and uterine cervix was separately carried out. The questionnaire on health and daily life including lifestyles was inquired distributing to the participants before the health examinations, and the answers were confirmed and revised by the trained health nurses at the time of the health examinations. The items of questions were personal and family medical histories, health status for recent two years living environment and health status of growth period, hygienic attitudes to daily life and periodical health check-up and reproductive history. Lifestyle habits including smoking habit (current smokers, ex-smokers and never smokers), alcohol drinking status (regular drinkers, irregular drinkers and non-drinkers) and dietary intake of major foods were inquired. These habitual intakes of major foods and drinks were recorded by frequency (five categories: daily, 3-4 times/week, 1-2 times/week, 1-2 times/month, and rarely). Preference of salty or fatty foods were also questioned. Occupational history/working conditions and years of schooling were asked to be described.

The sample sera at fasting were collected at the time of health examinations and immediately separated from blood cells by the centrifugation within one hour. The biochemical data of the sera were estimated using with the autoanalyzer (SMAC, Technicon Company Ltd.). Serum carotenoid concentrations were measured by the HPLC method, previously described, after being stored them at -80°C. Serum carotenoid level was categorized into three grades (three equal parts); high, moderate and low.

This cohort was followed up until the end of December 1994 to confirm their live or death, using mortality records from the Government, getting the permission from the Agency of General Affairs and Ministry of Health and Welfare. Death certificates were examined to confirm underlying cause of death and contributory ones. During the follow-up periods from 2-8 years, 98 deaths among the cohort (67 males and 31 females) were observed; 44 from malignant neoplasm (34 males and 10 females) including 10 stomach, 6 colon, 8 liver, 6 lung, 5 pancreas and 9 others, 13 from ischemic heart diseases (9 males and 4 females), 10 from cerebrovascular diseases (4 males and 6 females) and 18 from other diseases (11 males and 7 females), and 13 from accidents (9 males and 4 females). Mortality rates from all causes and from cancer by site between the groups with high, moderate and low serum levels of carotenoids were calculated and risks were estimated by the Cox's Proportional Hazard Model using the program of the SAS system for adjusting age, smoking habits and alcohol drinking status, which might affect serum level of carotenoids significantly.

**RESULTS**

Table 1 shows age and sex distribution of the subjects studied and their smoking habit, alcohol drinking status and intake frequency of green yellow vegetables. The CHEP was applied to the age group of more than 40, but those 39 years were accepted to participate in this program because they become 40 years old within the year. The age group of 39-49 years occupied about half of the subjects and that of 50-59 years was about third. The number of the subjects enrolled was about 20% of the relevant population in Y-town, and the age distribution was similar to the inhabitants of Y-town, although this cohort was not randomly selected in this town. The proportions of current smokers was 53.7% in males and 10.1% in females, and regular alcohol drinkers was 66.3% in males and 16.3% in females. The proportions of group with high frequency of intake of green yellow vegetables were 34.3% in males and 43.7% in females and those of lower frequency of intake were 30.1% and 18.1%, respectively. Females showed much intake frequency of green yellow vegetables than males.

Serum geometric mean values of carotenoids such as $\beta$-carotene, $\alpha$-carotene and lycopene for this cohort, were 0.397 $\mu$ mol/l (95% ranges: 0.093-1.402 $\mu$ mol/l) for males and 0.929 $\mu$ mol/l (0.302-2.379 $\mu$ mol/l) for females, 0.098 $\mu$ mol/l (0.024-0.324 $\mu$ mol/l) for males and 0.156 $\mu$ mol/l (0.037-0.466 $\mu$ mol/l) for females, and 0.300 $\mu$ mol/l (0.069-0.987 $\mu$ mol/l) for males and 0.425 $\mu$ mol/l (0.119-1.227 $\mu$ mol/l) for females, respectively. Each of carotenoid values was significantly higher for females than for males. The trends in serum carotenoid levels by age were shown in Figure 1. The serum $\alpha$-carotene concentration showed a stable trend with aging in both sexes, although their levels were low. Serum lycopene concentration tended a slightly decreasing with
Table 1. Characteristics of the follow-up subjects.

| Item                        | Males (%) | Females (%) | Total (%) |
|-----------------------------|-----------|-------------|-----------|
| Age                         | 39-49     | 740 (52.0)  | 1166 (49.6)|
|                             | 50-59     | 483 (33.9)  | 810 (34.4) |
|                             | 60-69     | 187 (13.1)  | 332 (14.1) |
|                             | 70-83     | 14 (1.1)    | 45 (1.9)   |
| Total                       | 929 (100.0)| 1424 (100.0)| 2353 (100.0)|
| Smoking habit               |           |             |           |
| current smoker              | 499 (53.7)| 144 (10.1)  | 643 (27.3) |
| ex-smoker                   | 202 (21.7)| 35 (2.5)    | 237 (10.1) |
| never smoker                | 228 (24.5)| 1245 (87.4) | 1473 (62.6)|
| Alcohol drinking habit      |           |             |           |
| regular drinker             | 616 (66.3)| 232 (16.3)  | 848 (36.0) |
| irregular drinker           | 59 (6.4)  | 23 (1.6)    | 82 (3.5)   |
| non drinker                 | 254 (27.3)| 1169 (82.1) | 1423 (60.5)|
| Intake frequency of green    |           |             |           |
| yellow vegetables            |           |             |           |
| high (>3-4 times/week)      | 319 (34.3)| 622 (43.7)  | 941 (37.1) |
| moderate (1-2 times/week)   | 330 (35.5)| 544 (38.2)  | 874 (34.4) |
| low (<1-2 times/month)      | 280 (30.1)| 258 (18.1)  | 538 (21.2) |

Each data was represented as the geometric mean value (μ mol/l).

Figure 1. Serum carotenoid levels by sex and age.

Aging, but those of age group of more than 70 years in females showed uprising. While slightly increasing trends were observed for β-carotene with aging in both sexes. The levels in the age groups more than 50 years have elevated significantly.

Serum β-carotene levels among current smokers and regular drinkers were significantly lower (0.266 μmol/l for males, 0.505 μmol/l for females) than those of never smokers and nondrinkers (0.713 μmol/l for males: p < 0.001, 1.006 μmol/l for females: p < 0.001), as shown in Figure 2 and 3. While α-carotene and lycopene showed little effects by smoking and drinking. The rates in reduction of the concentrations of carotenoids among the current smokers compared with never smokers were 41.6% in β-carotene, 29.2% in α-carotene and 22.3% in lycopene for males and 38.5%, 22.5% and 17.9% for females, respectively. A similar trend was found on those of β-carotene values for regular drinkers (males: 45.2%, females: 23.8%), compared with nondrinkers.
Each data was represented as the geometric mean value (μ mol/l) separated as follows; current smokers and regular drinker (n=356), current smokers and nondrinkers (n=108), ex-smokers and regular drinkers (n=139), ex-smokers and nondrinkers (n=47), never smokers and regular drinkers (n=121), and never smokers and nondrinkers (n=99).

Figure 2. Serum carotenoid levels for males by smoking and alcohol drinking habits.

Current smokers and regular drinkers (n=54), current smokers and nondrinkers (n=82), ex-smokers and regular drinkers (n=10), ex-smokers and nondrinkers (n=20), never smokers and regular drinkers (n=168), and never smokers and nondrinkers (n=1067).

Figure 3. Serum carotenoid levels for females by smoking and alcohol drinking habits.

Serum carotenoid levels were compared between the survivors at the end of 1994 and deaths during the observation period, as shown in Table 2. Three carotenoid levels were significantly higher in the survivors than those of the deaths in the
Serum \( \beta\)-Carotene Levels and Cancer Mortality Rates

Overall, females showed significantly higher levels of \( \beta\)-carotene and lycopene in the survivors than in the deaths from all causes, but males did not show. Cancer deaths showed similar tendency of the deaths from all causes in the overall cases, but only \( \beta\)-carotene level was significant in females.

Hazard ratios of serum carotenoid levels to death rates were shown in Table 3. Carotenoid levels were categorized into three groups (three equal parts), such as \( \beta\)-carotene: low

### Table 2. Comparison of serum carotenoid levels between the subjects alive and died in the follow-up residents.

| Carotenoid   | Sex    | Alive                  | All causes               | Cancer of all sites |
|--------------|--------|------------------------|--------------------------|--------------------|
| \( \beta\)-Carotene (\( \mu\) mol/l) | male   | 0.397 (0.100-1.360)    | 0.399 (0.061-2.263) ns   | 0.397 (0.115-2.282) ns |
|             | female | 0.933 (0.313-2.384)    | 0.732 (0.201-1.676) *    | 0.616 (0.201-1.563) * |
|             | overall| 0.674 (0.147-2.153)    | 0.484 (0.061-2.285) ***  | 0.440 (0.141-1.563) *** |
| \( \alpha\)-Carotene (\( \mu\) mol/l) | male   | 0.098 (0.030-0.315)    | 0.089 (0.037-0.466) ns   | 0.086 (0.037-0.466) ns |
|             | female | 0.157 (0.037-0.466)    | 0.119 (0.054-0.285) ns   | 0.123 (0.054-0.559) ns |
|             | overall| 0.132 (0.030-0.406)    | 0.099 (0.017-0.471) ***  | 0.093 (0.019-0.559) *** |
| Lycopene (\( \mu\) mol/l)      | male   | 0.300 (0.074-0.987)    | 0.279 (0.056-0.866) ns   | 0.271 (0.018-1.229) ns |
|             | female | 0.430 (0.123-1.229)    | 0.300 (0.095-1.693) **   | 0.318 (0.117-1.701) ns |
|             | overall| 0.374 (0.099-1.157)    | 0.285 (0.061-1.205) ***  | 0.283 (0.069-1.206) ** |

| Number       | male   | 862        | 67          | 34 |
|--------------|--------|------------|-------------|----|
|              | female | 1393       | 31          | 10 |
|              | overall| 2255       | 98          | 44 |

Data were represented as the geometric mean values and the ranges of 5%-95% in the parenthesis.

ns : not significant, * : p < 0.05, ** : p < 0.01, *** : p < 0.001.

### Table 3. Hazard ratio of mortality for all causes and cancer of all sites on serum carotenoid levels for the follow-up residents.

| Serum carotenoid | Residents | No. of survivors | No. of deaths | Mortality rates | H.R. (95% C.I.) |
|------------------|-----------|------------------|---------------|----------------|-----------------|
| \( \beta\)-Carotene (\( \mu\) mol/l) | male | 282 | 258 | 85.1 | 24 | 1 | 46.1 | 13 | 1 |
| low: males<0.266; females<0.682 | 350 | 328 | 62.9 | 22 | 0.65 (0.36-1.19) | 34.3 | 12 | 0.72 (0.32-1.62) |
| moderate: 0.266≤males≤0.592; 0.682≤females≤1.266 | 297 | 276 | 70.7 | 21 | 0.44 (0.22-0.85) | 30.3 | 9 | 0.36 (0.13-0.95) |
| high: males<0.592; females<1.266 | female | 401 | 387 | 34.9 | 14 | 0.54 (0.28-1.12) | 30.3 | 9 | 0.36 (0.13-0.95) |
|                | 568 | 560 | 14.1 | 0.33 (0.14-0.80) | 35.5 | 2 | 0.21 (0.04-0.16) |
|                | 455 | 446 | 19.8 | 0.47 (0.20-0.12) | 44.4 | 2 | 0.25 (0.05-0.13) |
|                | overall | 683 | 645 | 55.6 | 38 | 0.78 (0.40-1.99) | 19 | 1 | 1 |
|                | female | 918 | 888 | 32.7 | 30 | 0.53 (0.33-0.88) | 15.2 | 14 | 0.52 (0.26-1.07) |
|                | 752 | 722 | 39.9 | 30 | 0.46 (0.27-0.78) | 14.6 | 11 | 0.33 (0.14-0.75) |
| \( \alpha\)-Carotene (\( \mu\) mol/l) | male | 251 | 226 | 99.6 | 25 | 1 | 47.8 | 12 | 1 |
| low: males<0.065; females<0.108 | 405 | 384 | 51.9 | 21 | 0.54 (0.30-0.97) | 32.1 | 1 | 0.74 (0.32-0.58) |
| moderate: 0.065≤males≤0.151; 0.108≤females≤0.229 | female | 375 | 363 | 32 | 12 | 0.63 (0.28-1.41) | 4.9 | 3 | 0.39 (0.09-1.65) |
| high: males<0.151; females<0.229 | 614 | 602 | 19.5 | 12 | 0.47 (0.22-1.45) | 4.6 | 3 | 0.38 (0.08-2.07) |
|                | overall | 626 | 589 | 59.1 | 37 | 0.77 (0.41-1.49) | 17 | 1 | 1 |
|                | female | 1019 | 986 | 32.4 | 33 | 0.58 (0.36-0.92) | 15.7 | 16 | 0.62 (0.31-1.23) |
|                | 708 | 680 | 39.5 | 28 | 0.79 (0.48-1.31) | 15.5 | 11 | 0.65 (0.35-1.62) |
| Lycopene (\( \mu\) mol/l) | male | 275 | 255 | 72.7 | 20 | 1 | 43.6 | 12 | 1 |
| low: males<0.201; females<0.300 | 359 | 331 | 78 | 28 | 1.16 (0.56-2.06) | 36.2 | 13 | 0.92 (0.42-2.03) |
| moderate: 0.201≤males≤0.449; 0.300≤females≤0.605 | female | 295 | 276 | 64.4 | 19 | 0.98 (0.52-1.84) | 30.5 | 9 | 0.80 (0.33-1.93) |
| high: males<0.449; females<0.605 | 402 | 384 | 44.8 | 18 | 0.38 (0.16-0.87) | 3.6 | 2 | 0.27 (0.06-1.33) |
|                | overall | 677 | 639 | 56.1 | 38 | 0.78 (0.30-1.24) | 26.6 | 18 | 1 |
|                | female | 909 | 873 | 39.6 | 36 | 0.78 (0.30-1.24) | 16.5 | 15 | 0.71 (0.36-1.41) |
|                | 767 | 743 | 31.3 | 24 | 0.68 (0.41-1.14) | 14.3 | 11 | 0.67 (0.32-1.44) |

The hazard ratio (H.R.) and the confidence interval (C.I.) were calculated by adjusting with age, and habits of smoking and alcohol drinking.

No. of deaths in the subjects: all death- 98 (67 males and 31 females), cancer - 44 (34 males and 10 females).

Mortality rate = [No. of deaths/ No. of total] \times 1000.
Table 4. Hazard ratio of mortality for all causes and cancer of all sites on smoking habit for the follow-up residents.

| Item                          | No. of Residents | No. of survival | Mortality rates | No. of deaths | All causes (H.R.95% C.I.) | Mortality rates | No. of deaths | Cancer of all sites (H.R.95% C.I.) |
|-------------------------------|------------------|-----------------|-----------------|---------------|---------------------------|----------------|---------------|-----------------------------------|
| Smoking habit                 |                  |                 |                 |               |                           |                 |               |                                   |
| 1) current smokers            | male             | 497             | 465             | 68.4          | 34            | 1                          | 40.2           | 20            | 1                                 |
|                               | 198              | 184             | 90.9           | 18            | 0.90 (0.50-1.59) | 50.5           | 10            | 0.80 (0.37-1.71) |
|                               | 228              | 213             | 65.8           | 15            | 0.68 (0.36-1.27) | 17.5           | 4             | 0.29 (0.10-0.86)  |
| 2) ex-smokers                 | female           | 154             | 141             | 84.4          | 13            | 1                          | 13             | 2             | 1                                 |
|                               | 35               | 32              | 85.7           | 3             | 2.14 (0.48-12.05) | 0              | 0             | -                                 |
|                               | 1245             | 1220            | 20.1           | 25            | 0.71 (0.21-2.43) | 6.4            | 8             | 0.31 (0.06-1.53) |
| 3) never smokers              | overall          | 643             | 606             | 57.5          | 37            | 1                          | 34.2           | 22            | 1                                 |
|                               | 237              | 216             | 88.6           | 21            | 0.98 (0.57-1.68) | 42.2           | 10            | 0.76 (0.36-1.62) |
|                               | 1473             | 1433            | 27.2           | 40            | 0.63 (0.36-1.10) | 8.2            | 12            | 0.32 (0.13-0.77) |

The hazard ratio (H.R.) and the confidence interval (C.I.) were calculated by adjusting with age, and habits of alcohol drinking. No. of deaths in the subjects: all death- 98 (67 males and 31 females), cancer - 44 (34 males and 10 females). Mortality rate = [No. of deaths/ No. of total] × 1000.

group less than 0.266 μmol/l in males and less than 0.682 μmol/l in females and high group: more than 0.592 μmol/l in males and more than 1.266 μmol/l in females. Serum α-carotene and lycopene levels were categorized similarly. Mortality rates were higher in the groups with low serum carotenoid groups for these observation period, but lower in the groups with high serum carotenoid levels. Moderate level groups showed similar rates to those of high levels. Lower hazard ratios were observed in the groups with high serum carotenoid levels. Statistically significant low hazard ratios for all causes and cancer deaths were observed in the overall cases, and in males with high α-carotene and β-carotene levels for all causes. Females showed similarly low hazard ratios in the groups with moderate levels of β-carotene and lycopene for all causes, but did not for cancer deaths.

Hazard ratios related to smoking habits and mortality rates were also computed adjusting age and alcohol drinking status, as shown in Table 4. A significantly low hazard ratios were observed in the never smoker group for cancer deaths compared with those of current smokers in males and the overall cases. No significant differences were observed in other groups. Hazard ratios for alcohol nondrinkers in the overall were lower for regular drinkers (hazard ratio of all causes: 0.80, 95% C.I.: 0.49-1.31, hazard ratio of cancer deaths: 0.85, 95% C.I.: 0.41-1.75), but not significant. High intake frequency of green yellow vegetables (more than 3-4 times/week) was also not significantly associated with mortality rates (hazard ratio of all causes: 0.93, 95% C.I.: 0.57-1.52, hazard ratio of cancer deaths: 0.84, 95% C.I.: 0.40-1.76) in any groups after controlling for age, smoking habit and alcohol drinking status.

DISCUSSION AND CONCLUSION

The aim of this study was to confirm whether lower death rates of cancer or all causes among those inhabitants with high serum β-, α-carotenes and lycopene levels, compared with those with low levels could be observed or not. A total of 2353 subjects were enrolled in this cohort. They were not randomly selected in Y-town, but their residence areas were scattered in all town, not clustered in a specific area and the distributions by sex and age were similar to that of all inhabitants. History of previous diseases, dietary habits and other lifestyles showed no difference between this cohort and general population. All 2353 cases could be followed up until the end of 1994. All subjects were diagnosed as healthy at the time of enrollment and a fraction of total deaths during observation period was small, less than 5%, while the inhabitants removed, except for the young were small and the numbers of the death were reliable. So, we had calculated sample death rates and did not use person year rates.

Serum levels of carotenoids were measured using the same equipment during this study period. The results were checked using the pooled sera stored at -80 degree C as the reference, avoiding the biases in measurements. Serum mean values and sex differences of carotenoids such as β-carotene, α-carotene and lycopene in this residents were almost agreed with those of the other inhabitants. In addition, the lower values of serum carotenoids for current smokers and regular alcohol drinkers were also confirmed in this study as those of the other reports. A significant positive association between mortality rate of cancer deaths and smoking habit was found in the overall cases in this study. However, mortality levels among regular alcohol drinkers, and between those with high and low intake frequency of green yellow vegetables included spinach, carrot, pumpkin, tomato, green leaf vegetables, etc. in this study, which affected with serum levels of these carotenoids did not show significant associations. Mortality rates affected with many other factors, so the above results need to further study in the large cohort. A reverse association between mortality rates of all causes or cancer and high serum β-carotene levels could...
be observed under controlling with age, smoking habit and alcohol drinking status, as same level as those already reported 14,16-18. While no significant association with high serum levels of α-carotene and lycopene, and mortality rates of cancer deaths was also apparently found in the overall cases under adjusting with sex, age, habits of smoking and alcohol drinking. It should be noted that the number of the cohort was not large, so that the observation period seemed to be short. It might be one of reasons for some inconsistent data.

Recent intervention study showed the reduced cancer death rate such as stomach cancer in Chinese rural inhabitants administered with the mixed β-carotene, α-tocopherol and selenium 30. The hazard ratio of stomach cancer in our study was lower as 0.45 (95% C.I.: 0.73-2.78) calculated using with 10 stomach cancer deaths adjusted with sex, age, smoking habit, alcohol drinking status and intake frequency of green yellow vegetables, as the results was not significant.

Mechanism of carcinogenesis is considered as complex and carotenoids may be one of the causal factors. It is already shown that β-carotene has a role of antioxidant activity and the enhancement of immunity related to carcinogenesis 32,34,38. It was indicated that carotenoids might protect from oxidative stress, as attack on lipid membranes and damage to various membranes, enzymes and nucleic acids by activated oxygens and free radicals 32-34. One of the other factors reported that peripheral blood concentrations of lymphocyte subsets, related with immune system for cancer prevention, such as T cells (T4,T8), except for NK cells (Leu7), were not apparently associated with serum β-carotene levels 38, as same as other reports 30,39,40. Although carotenoids were enhanced the proliferation of T and B cells and NK cells and reduced the development of the tumor cells in the animal experiments 34,38-40, the mechanism of immune system for cancer prevention also was not yet clear. Moreover, the results revealed that serum β-carotene levels were inversely and strongly associated with serum lipid peroxide levels in this residents, comparing to serum levels of α-carotene and lycopene 40, as corresponding with the inverse association with the cancer death rates. This results should be studied further because some reports showed activity of antioxidants and/or immunity are stronger for lycopene than for β-carotene in vitro study 42-44.

In conclusion, this study suggests that β-carotene from foods is associated with some protective effect on cancer deaths.

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