

Cancer Epidemiology in Japan

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Patterns, change in occurrence, causative risk factors, and control strategy for cancer of each site in Japanese populations were studied by applying standard methods and techniques of biostatistics and epidemiology. As the results, cancers in Japan were classified into two groups: one on the decrease (stomach, cervix) and the other on the increase (lung, colon, pancreas, breast, prostate, urinary organs, leukemia). Analysis of vital statistics, national nutrition survey data, and on-going prospective study data revealed change in selective dietary intake and increase in cigarette consumption are the major factors responsible for such trend. Epidemiological characteristics and major risk factors of cancers of stomach, colon, pancreas, lung, breast, uterine cervix, ovary, endometrium, prostate, urinary bladder, and leukemia in Japan were summarized. A limited effect of mass screening was observed in the case of stomach cancer in addition to the strong effect of diet and nutrition.

Cigarette smoking was confirmed to be the major causative factor of lung cancer in Japan. A close association of increased intake of animal fat and breast cancer risk in Japanese women was also observed.

In Japan, the pattern of cancer has been changing rapidly in recent years. Cancers of the stomach and cervix have shown a steep downward trend, whereas cancers of the lung, pancreas, intestine, prostate, ovary, breast, urinary organs, and leukemia have been increasing steadily. One of the most impressive changes has been the decrease in stomach cancer mortality.

Factors possibly related to the changing trend for these selected cancers will be reviewed.

Materials and Methods

Vital statistics in Japan from 1955 to 1977 and results of the National Nutritional Survey from 1949 to 1976 provided the data for this presentation. Standard methods of both descriptive and analytic epidemiology were fully utilized in analyzing the data, in particular, the preliminary results of the population prospective study in Japan currently being carried out by this author.

Results and Discussion

General Observations

The age-adjusted death rates (adjusted to 1935 census population in Japan) for cancer of all sites

show almost no increase in males in the last decade. In females, even a slight decrease was observed. The steepest decrease was noted for cervical cancer and next for stomach cancer (in both males and females). On the other hand, a sharp increase was observed for cancers of the lung, pancreas, prostate, urinary organs, colon-rectum, liver, breast, ovary, and leukemia. Similar tendencies have been observed in incidence rates in selected cancer registries such as in Osaka and Miyagi.

To study the underlying mechanism of the decrease, correlation coefficients of the death rates in Japan, 1950-75, for selected age groups were calculated between cohort pairs and calendar-year pairs. In case of stomach cancer, a calendar-year effects were far stronger than cohort effects, partial correlation coefficient between ages 40-44 and 60-64 being +0.75 and -0.09 in males and +0.87 and +0.37 in females, respectively (*1*). A similar tendency was observed for breast cancer. However, strong cohort effects were observed for lung and cervical cancer (*1*).

Stomach Cancer

The age-specific death rate for stomach cancer has been declining since 1955. Among males, the death rate in 1977 in the 40-44 age group was 39% lower than it was in 1955. The decline was 42%, 44%, 41%, 39%, and 32% for the age groups 45-49, 50-54, 55-59,

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60-64, and 65-69, respectively. In females, the decline was 30%, 34%, 40%, 42%, and 39% for the age groups 40-44, 45-49, 50-54, 55-59, 60-64, and 65-69, respectively. The decline was most striking for cancer of the pylorus and far less so for cancer of the cardia; furthermore, it was most striking in metropolitan areas, next in other cities, and least in counties. The decline was observed for most occupational groups except for sales workers (2).

As the decrease in the stomach cancer death rate was considered due mostly to calendar-year effects rather than cohort effects, yearly changes in selected environmental conditions were studied. Although considerable differences still exist between the nutritional intake of the Japanese people as compared to people in the United States, there has been a striking change in diet in Japan since 1949; this change is clearly demonstrated by the National Nutritional Survey (3). The consumption of milk and milk products showed a 24.5-fold increase from 1949 to 1976. The ratios of the increase in consumption of other food items are as follows: meat, 11.9; eggs, 12.6; oil, 9.4; fruits, 6.2. Comparatively little change was observed in the consumption of fish, vegetables, and rice. A series of retrospective studies (4-6) and also ongoing prospective studies (7) for 265,118 adults aged 40 years and above in 29 Health Center Districts in Japan on the relationship of diet to stomach cancer clearly showed a significantly higher risk in both males and females who are daily cigarette smokers, a significantly higher risk in those eating salty foods such as pickles and fish in every meal, and a significantly lower risk of stomach cancer among those who drink two glasses of milk daily.

The relative risk of stomach cancer in daily smokers compared to nonsmokers was 1.58 in males. Although this was much lower than the relative risk of lung cancer, which was 3.76, the absolute magnitude of excess deaths among daily cigarette smokers was far higher for stomach cancer than for lung cancer, i.e., 60.13 and 45.91, respectively. The attributable risk percent related to daily cigarette smoking for stomach cancer was 30.1%, whereas it was 67.2% for lung cancer (1).

Daily cigarette smoking is thus important as one of the risk factors for stomach cancer and of particular significance in explaining the reason for the consistent preponderance of males in the number of reported stomach cancer cases. The relative risk is similar to those found in prospective studies reported in the literature: 1.45 in seven studies (8).

That daily cigarette smoking is a risk factor in stomach cancer is also significant in that it provides human evidence that the intake of selected extrinsic chemical carcinogens can surely increase the risk of stomach cancer, and an intensive search must be

undertaken for such carcinogens in our daily environment or life-style, particularly in our food.

Thus if people were to stop smoking cigarettes, the risk for stomach cancer would surely go down further, and the slope of the decline in Japan would become even steeper. The much lower decreasing ratio of the mortality rate for cancer of the cardia of the stomach (2) can be explained by the fact that the promoting effect of cigarette smoking is strongest for cancer of the cardia, the relative risk being 1.86 in cardia and 1.23 in pylorus (1). The dose-response relationship is clearer in cancer of the cardia.

However, neither the intercountry variation nor the decreasing trend in the stomach cancer death rate in general appears to be explained by the smoking factor. The difference or change in dietary pattern must be far more important in explaining such geographic variation and the overall downward trend in stomach cancer mortality. Observed higher risk in those taking foods of high salt concentration should be interpreted along this line. With the growing use of electric refrigerators, consumption of such salty preserved foods has decreased steadily, while consumption of milk and milk products has been on an upward trend.

The recent decline in stomach cancer in Japan should be interpreted mostly as a reflection of such dietary improvements. The extent of the decrease, which should be attributed to the effect of a nationwide early detection program in recent years, is difficult to assess, although the age groups in which stomach cancer mortality markedly decreased correspond to the age groups for which a current mass screening program was undertaken (9). Early detection programs for stomach cancer have been carried out widely since 1960. The number of people examined for stomach cancer by mass radiography and the number of cases detected in 1975 were 3,087,031 and 3,022 respectively. The five-year survival rate in patients whose cases were detected by such mass screening is known to be significantly higher than the survival rate in the unscreened group. A follow-up of screened persons clearly showed a significant reduction in the stomach cancer adjusted death rate compared to that in unscreened persons, 144.32 out of 33,865 screened person-years and 176.82 out of 388,715 unscreened person-years, respectively (study in Kanagawa Prefecture 1962-1971). Similar results have been reported from Tottori (99.3 in screened group vs. 255.2 in unscreened group) and from Osaka (162.4 in screened group vs. 255.2 in unscreened group) (8). It should be noted, however, that none of these were randomized trials.

The decline in the age-specific mortality rate for stomach cancer was studied in 46 prefectures in Japan. These prefectures were classified into four

groups according to the consistency and the extent of the decline in the stomach cancer mortality rate in the 40-74 age group. The extent of decline in the age-specific stomach cancer death rate was most striking in prefectures where the rate of screening by mass gastrography was high. The extent of decline was highest when both the consumption of milk and eggs and the rate of screening were higher than the national average (8). Here also, attention should be paid to the fact that both of these factors were related to the economic level of each prefecture. In summary, the recent decline in stomach cancer mortality in Japan could be interpreted as a reflection of dietary improvement in Japan, just as in other developed countries, influenced partly by the effect of early detection. The influence of general affluence can also not be excluded.

Colon Cancer

For many years, colon cancer occurred only quite infrequently in Japan, but, based on both mortality and morbidity statistics, the disease is now apparently on the increase. The age-specific mortality rate for colon cancer clearly has been increasing steadily in recent years in Japan. The CR ratio (colon/rectum ratio) was calculated by sex and by years, both for mortality statistics and for morbidity statistics. The following results were obtained.

The CR ratio is higher in females than in males. (1.09 and 0.86, respectively, in 1973). The CR ratio has been continuously increasing both in males and females, the slopes being quite similar. The ratio was 0.77 in females and 0.57 in males in 1955. Among the different anatomical sites of the intestinal tract, cancer of the sigmoid colon showed the highest increasing ratio, 1.77 in males and 2.11 in females, when 1973 mortality figures were compared to 1968 figures. The trend of the CR ratio is on the increase both in Japan and in U.S. whites, again the slopes being quite similar.

The 10-year follow-up results of the prospective epidemiologic study for a large adult population in Japan (1965-1975) showed that the CR ratio tends to be higher in those who consume a smaller amount of rice daily; a significant reverse association was observed between the amount of daily rice intake and the CR ratio, the ratio being 0.71 in males and 1.05 in females for those consuming four cups of rice or less a day, and 1.59 and 1.81, respectively, for those consuming six cups of rice or more a day.

However, our ongoing prospective study showed no elevated standardized mortality ratio for colon cancer in daily meat consumers. Neither smoking nor drinking is strongly associated with colon cancer.

Cancer of the Pancreas

Our prospective study clearly showed that the risk for pancreatic cancer is high in daily cigarette smokers, relative risk and attributable risk being 1.41 and 23.3%, respectively, and in daily meat consumers, relative risk and attributable risk being 2.54 and 11.4% respectively. The risk was highest when these two factors were combined. The consumption figures for both have been increasing rapidly in Japan in recent years. The striking increase in pancreatic cancer, therefore, must be a reflection of the increase of these two factors.

Lung Cancer

Lung cancer mortality has been increasing rapidly. Until a few years ago, the number of deaths in Japan from pulmonary tuberculosis was far higher than that from lung cancer. As recorded in 1947, the death toll due to pulmonary tuberculosis was 121,912, which is 159 times that for cancer cases (768). This figure has decreased each year. In 1972, the number of tuberculosis deaths (11,983) was lower than the number of lung cancer deaths (12,290) (10). The figures were 8,803 and 17,235, respectively, in 1977. If the current pace continues, the death rate for lung cancer is expected to catch up soon with that for stomach cancer.

Daily cigarette smoking showed up as the most important cause of lung cancer in the ongoing prospective study, the relative risk and attributable risk being 3.76 and 67.2%, respectively, in males (1). A dose-response relationship was also clearly observed. Those who started smoking at a younger age tended to show a higher death rate for lung cancer. The recent increase in lung cancer morbidity and mortality rates can be interpreted, therefore, as a reflection of the sharp increase in per capita cigarette consumption in recent years in Japan, although a certain part of it could also be influenced by occupational factors, such as those experienced by metal workers (13). SMR for lung cancer was observed to be 17%, 54%, and 61% lower in those with daily intake of green-yellow vegetables in smokers, non-smokers and ex-smokers respectively, suggesting the existence of a protective effect of vitamin A and/or vitamin C.

Breast Cancer

Breast cancer is known to be infrequent in Japan. However, both mortality and morbidity rates for breast cancer have increased sharply in the last 20 years. A 63% and 54% increase in the mortality ratio was observed in women of the age groups 50-54 and 55-59 respectively. This increase was most striking

in metropolitan areas, less in cities, and lowest in counties (14).

There are two possible reasons for the recent increase in the breast cancer mortality rate. The first is the decline in birth rate. The birth rate (per 1,000) in Japan was 34.3 in 1947, 28.1 in 1950, 19.4 in 1955, and 15.5 in 1977. As the breast cancer incidence rate is known to be negatively correlated with birth rate, such a sharp decline in birth rate could be a reason for the recent increase in breast cancer mortality in Japan.

Another possible reason is the promoting influence of diet, in particular of dietary fat, the intake of which is increasing rapidly. This was shown clearly by our ongoing prospective studies. A significantly higher standardized mortality ratio of breast cancer in women with a habit of daily meat intake was observed, the SMR being 1.85 compared to non or occasional meat consumers. The SMR was 1.26 in the 40-54 age group and 2.38 in the 55 and over age group. This was also shown by a high correlation coefficient ($r=0.842$) between dietary fat intake and the breast cancer adjusted mortality rate in 12 districts in Japan. Such a high correlation coefficient was not observed for any other nutritional element (14). The intake of dietary fat (grams/capita/day) in Japan and in the United States in 1973 was 52 and 155, respectively, and 23 and 143, respectively, in 1957-1959 (2). Among all the nutritional elements, dietary fat intake has shown the most striking increase in Japan in recent years. It is of interest to note that the breast cancer mortality rate expected for the United States by extrapolating from the regression line of dietary fat-breast cancer correlation in Japan was 20 per 100,000 (adjusted to 1960 population in Japan) and the actual rate was 18 (14).

Among several food items, the highest correlation was found with per capita amount of pork intake ($r=0.895$); next came the amount of intake of animal fat such as lard ($r=0.675$). The partial correlation study revealed a nearly total disappearance of the high correlation between breast cancer mortality rate and dietary fat intake when the effect of pork intake was taken out. Pork appears to be the major source of dietary fat elevating the risk of breast cancer in Japan.

Cancer of the Uterine Cervix

The most striking downward trend is noted in the incidence and death rates for cancer of the cervix. The possible reasons for such steep decline must include (a) the upgrading of personal hygiene due to the improvement of home facilities such as bath and shower; (b) the tendency to postpone marriage to a later age; (c) the spread of birth control practices;

and, to some extent, (d) the improvement in nutrition, such as vitamin A intake. The age-adjusted death rate in 12 districts in Japan (1975) correlated negatively with the per capita intake of vitamin A (1970) ($r=-0.835$).

Cancer of the Ovary and Endometrium

These two cancers are definitely on the increase. The possible reasons, at least in part, must be common with those for the increase in breast cancer, in particular with regard to body size and diet.

Cancer of the Prostate

It is speculated that the reason for this increase is related to the change to a westernized diet. The occurrence of the disease was noted to be significantly less in vegetarians in our prospective study. The 10-year follow-up study of 122,261 men aged 40 years and above, which constitute 94.5% of the census population of 29 Health Center Districts, revealed a significantly lower age-standardized death rate for prostate cancer in daily ingesters of green yellow vegetables. This association is consistently observed in each socioeconomic class, in each prefecture and in each age group except age over 70. Selected epidemiologic phenomena such as the upward trend of the prostate cancer death rate in Japan, intracountry variation of death rate, the significantly lower incidence rate in Japan as compared to that of the U.S., and elevated risk in Japanese migrants to Hawaii appear to be explained by the variation in diet and change in amount of green-yellow vegetables ingested. The possible role of vitamin A is considered as a factor in preventing and inhibiting growth of prostate cancer. Most of the other factors studied appear noncontributory, except for marital status, where a higher risk was observed in "ever married" men.

Cancer of the Urinary Bladder

The tendency of increase is clear for males. A significant relationship was observed between daily cigarette smoking and urinary bladder cancer deaths, the relative risk and attributable risk being 1.36 and 21.3%, respectively (1). The reason for an increase in the bladder cancer death rate, at least in part, must be due to the increase in per capita cigarette consumption in recent years. Part of the increase could also come from occupational factors, such as benzidine exposure.

Leukemia

The ratio of increase in the leukemia death rate is

most striking after age 40, both in males and females, especially since 1965. Occupational and other environmental risk factors including diagnostic x-ray are now under study.

Summary

Trends in cancer mortality can assist in the interpretation of etiology. This is especially true in Japan where environmental conditions have been changing remarkably (15). Cancers of selected sites are classified into two major groups: those showing a downward trend and those showing an upward trend.

The downward trend of cancers of the stomach and cervix is similar to the trend found in United States whites, as well as in most western countries. Both of these diseases are known to be more common in persons from lower socioeconomic strata. Both dietary conditions and personal hygiene have changed in recent years in Japan, paralleling the economic development of the country and the increasing standard of living. The decrease in mortality for cancer of the stomach most probably reflects changes in risk factors such as dietary habits. In the case of cervical cancer, the decrease may be attributable to upgrading of personal hygiene and nutritional status and also to mass screening programs for early detection.

The upward trend in rates for cancers of certain sites shows Japanese rates approaching the rates of United States whites. The first group of such cancers is the smoking-related cancers, and the second group constitutes those cancers possibly related to diet. Both type of cancers will continue to increase as the consumption of both cigarettes and dietary fats is on a sharp increase in Japan.

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