Special Lecture

Epidemiology and Prevention of Breast Cancer in the 21st Century

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The incidence and mortality of breast cancer are high in Western industrialized countries and relatively low in Japan and other Asian countries. In Japan the incidence and mortality of breast cancer have gradually been increasing. Marrying later, having fewer children, a larger intake of fat, dairy products and meats and a larger body mass index in menopausal women may be related to the increased incidence of breast cancer in Japan. A review of risk factors identified from recent epidemiological studies in Japan indicates that obesity after 50 years of age is an important risk factor for postmenopausal breast cancer. Future estimations of cancer mortality and incidence predict that breast cancer will further increase to become a leading cancer in Japan in the 21st century.

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Breast Cancer Mortality and Incidence in Japan

There were 8393 breast cancer deaths in 1997 in Japan, accounting for 7.7% of cancer deaths in women. Breast cancer was the fifth most common cancer following stomach, colo-rectal, lung and liver cancers[1]. The estimated number of breast cancer cases in 1993 was 27 563 accounting for 14.3% of all sites. Breast cancer was the third most common cancer following stomach cancer and colo-rectal cancers[2]. The incidence/mortality ratio of breast cancer in 1993 was 4.0.

International Comparison of the Breast Cancer Mortality

The mortality and incidence of breast cancer are high in Western industrialized contries and relatively low in developing contries in Asia and other parts of the world. Figure 1 shows the age-adjusted mortality rates of 28 countries in 1987-1992[3]. The mortality of breast cancer is high in United Kingdom, Denmark, Ireland, the Netherlands and some other northern European contries, whereas the mortality is low in Japan, Mexico, Chile, Greece and some other countries in Eastern Europe. Figure 2 shows trends over time of the age-adjusted mortality of breast cancer from 1953-1957 to 1988-1992 for 28 countries[3]. The mortality of breast cancer has stabilized in countries with high mortality in the past and has

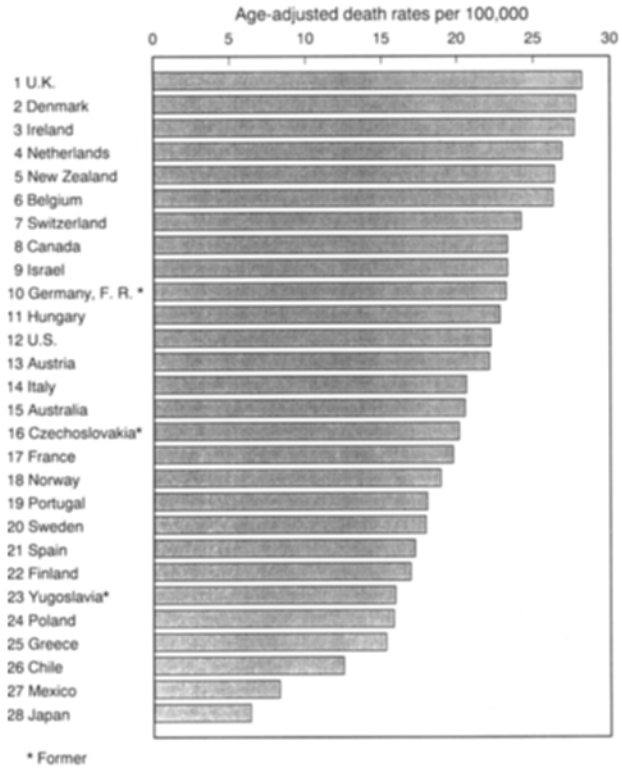

Fig 1. Age-adjusted death rates* of breast cancer in 28 countries (1988-1992). *Standardized, based on the World population. Data source: Kuroishi *et al* (1998)[3].

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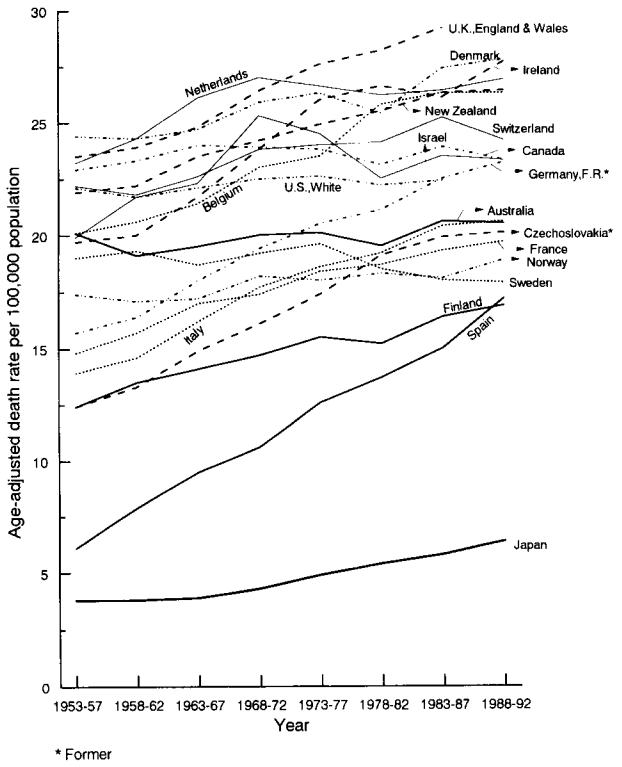

Fig 2. Trends in the age-adjusted death rate* of breast cancer for selected countries (1953-1957 to 1988-1992). *standardized, based on the World population. Data source: Kuroishi *et al* (1998)[3].

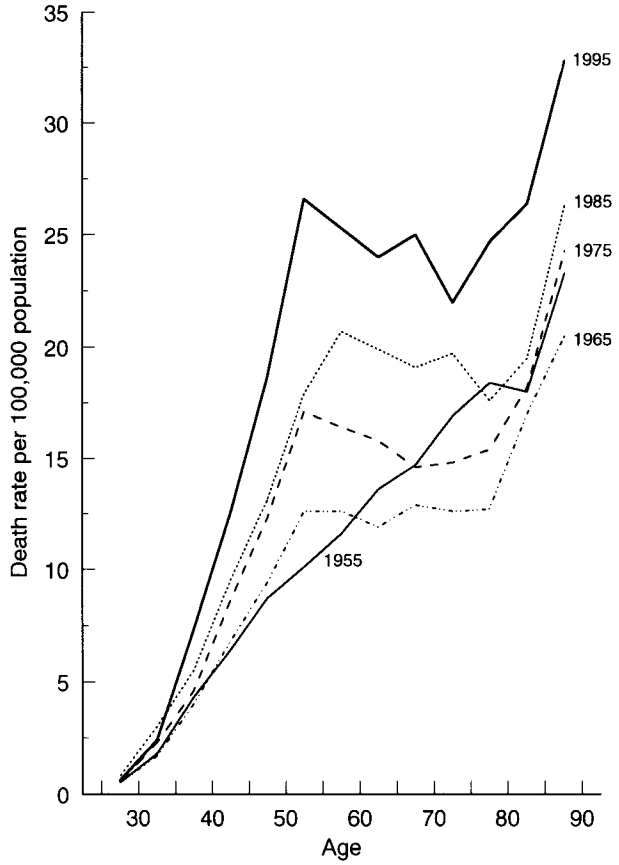

Fig 3. Trends in the age-specific death rate of breast cancer in Japan (1955,1965,1975,1985 and 1995). Data source: Kuroishi *et al* (1999)[4].

been increasing in countries where the mortality was previously low. A marked increase in breast cancer mortality can be observed in Spain and Czechoslovakia. The mortality in Japan has gradually been increasing, but is still much lower than in other countries.

Trends in Breast Cancer Mortality and Related Factors in Japan

Figure 3 shows age-specific death rates for 1955, 1965, 1975, 1985 and 1995[4]. An increase in mortality is most markedly observed in the 50- to 70-year old age group.

To study the possible reasons for increasing breast cancer mortality in Japan, several factors possibly related to the cause of breast cancer were examined (Fig 4)[5]. The results in Fig 4 clearly show that a decrease in the number of children, marrying at a later age, increased consumption of fat and meat, and increased body mass index in postmenopausal women are compatible with the increasing incidence of breast cancer.

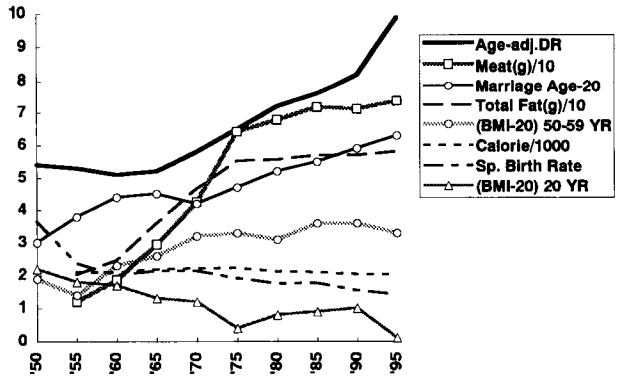

Fig 4. Trends in age-adjusted mortality and related factors in Japan (1950-1995). Data source: Vital statistics of Japan (1998)[5].

Geographical Distribution of Breast Cancer and Related Factors in Japan

Figure 5 shows a map of the standardized mortality ratio (SMR) of breast cancer by prefecture in 1995[4]. The mortality from breast cancer was high in Tokyo and some other prefectures with large metropolitan cities. Figure 6 shows trends in the age-adjusted mortality of breast cancer by municipality size and indicates that breast cancer mortality was highest in urban areas (10 large cities) and lowest in rural areas (counties). The

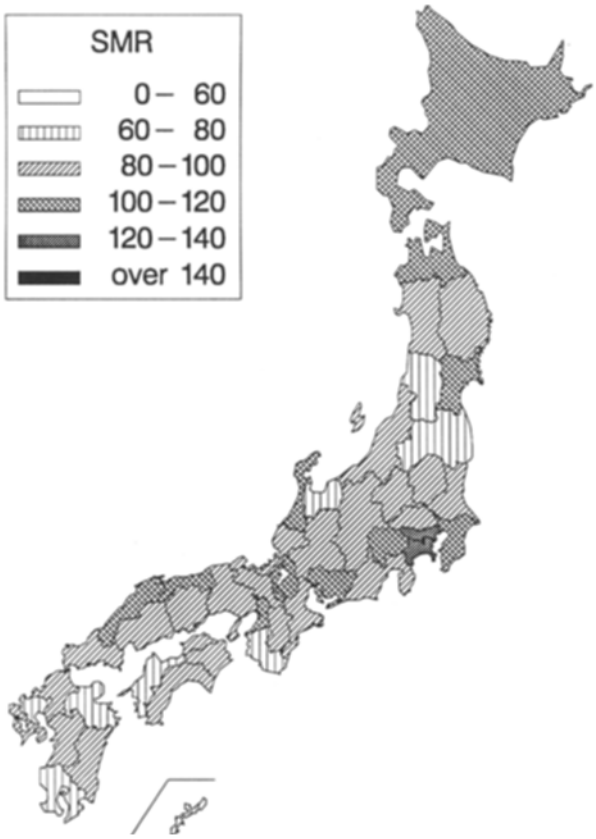

Fig 5. Maps of the standardized mortality ratio (SMR) of breast cancer by prefecture (1995). Data source: Kuroishi *et al* (1999)[4].

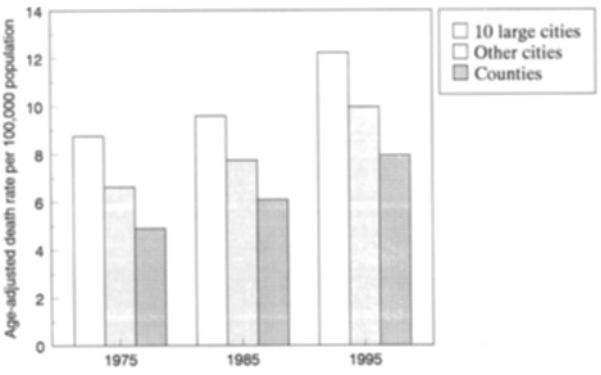

Fig 6. Age-adjusted death rates of breast cancer for 10 large cities, other cities and counties (1975, 1985 and 1995). Data source: Kuroishi *et al* (unpublished).

trend of increasing breast cancer mortality was the same in all areas.

Recent Results of Immigrant Study of Breast Cancer

From many studies[6-11] of immigrants the influence of some environmental factors has been implicated. Figure 7 shows the age-adjusted incidence rates of breast cancer for Chinese, Japanese and Caucasians in the United States. The original data were obtained from volume Ⅶ of "Cancer Incidence in Five Continents"[12]. Japanese and Chinese living in their native countries or other Asian countries show a low incidence of breast cancer, whereas Japanese and Chinese living in the United States show a much higher incidence rate, close to that of Caucasians in the United States. These results suggest the influence of some environmental factors, possibly diet and especially high fat intake, on the incidence of breast cancer.

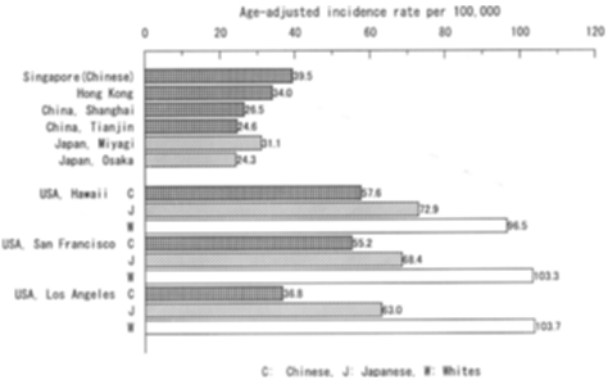

Fig 7. Comparisons of the age-adjusted incidence rate of breast cancer among Chinese, Japanese and Caucasians in the United States (1988-1992). Date source: Cancer Incidence in Five Continents, Vol Ⅶ (1997)[12].

Future Predictions of Breast Cancer in Japan

Kuroishi *et al* have predicted the future mortality from selected types of cancer in Japan through the year 2015 by extrapolating from the past trends of sex and age-specific mortality (Fig 8)[13], as have Kitagawa *et al* predicted the future incidence of cancer (Fig 9)[14]. According to their predictions, both the mortality and incidence of breast cancer will increase in the future in Japan, but the incidence will more markedly increase. The age-adjusted incidence rate of breast cancer will exceed that of stomach cancer by the year 2000 (Fig 9).

Risk Factors of Breast Cancer

From previous epidemiological studies many kinds of risk factors for breast cancer have been identified such as family history of breast cancer, history of benign breast disease, rapid growth, lower age at menarche, higher age at menopause,

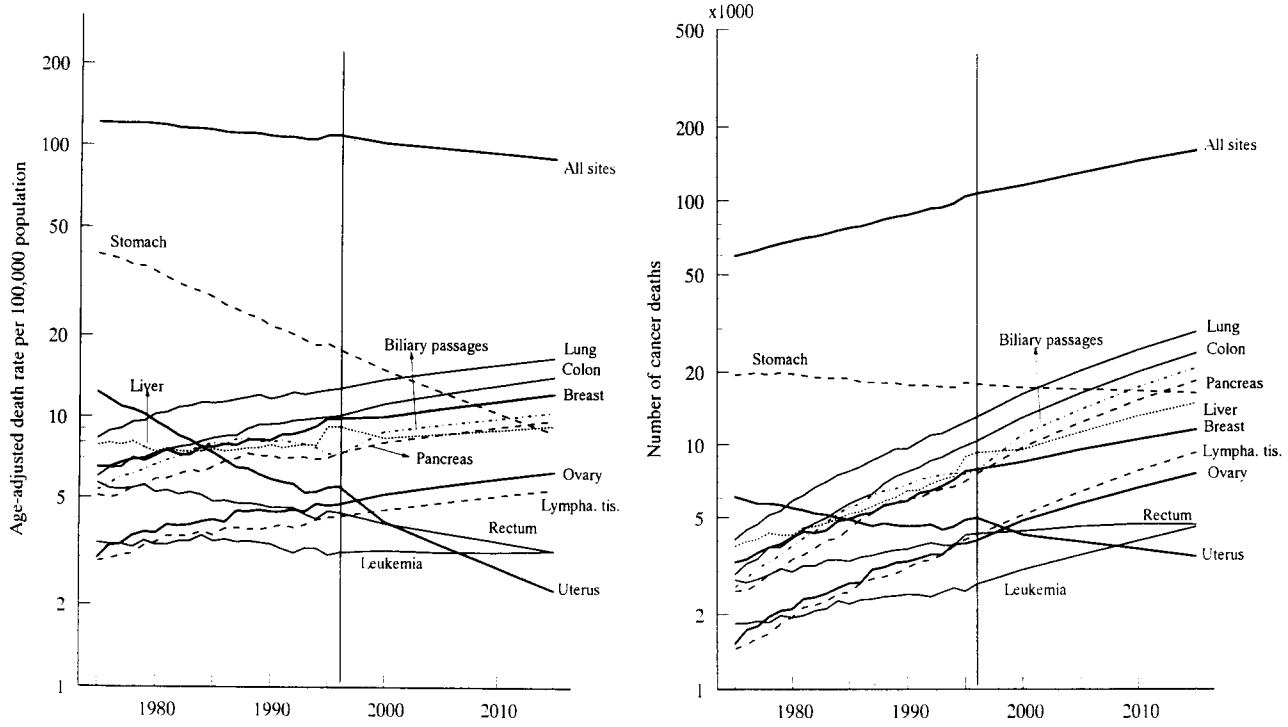

Fig 8. Prediction of cancer mortality by type through the year 2015 in Japan. Date source: Kuroishi *et al* (1999)[13].

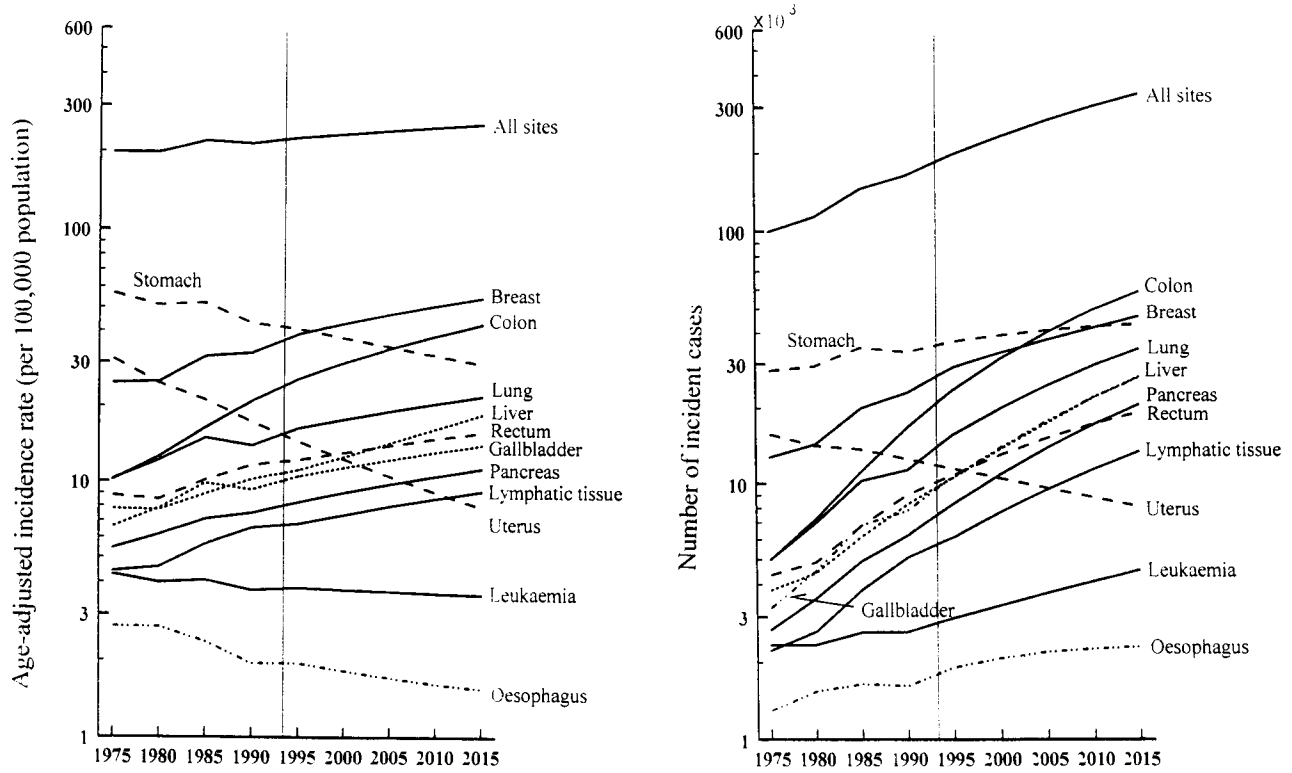

Fig 9. Prediction of cancer incidence by type through the year 2015 in Japan. Date source: Kitagawa *et al* (1994)[14].

higher age at first pregnancy and delivery of the first child, no history of lactation, small number of children, large intake of fat and meat, alcohol consumption, obesity after 50 years of age, radiation, less physical activity, etc[15-17]. From a large epidemiological study conducted at the Aichi Cancer Center involving 1052 cases of breast cancer and 23 163 cancer-free controls[18], a family history of

breast cancer and a high age at the first full-term pregnancy (27 years and over) were risk factors for the development of both pre- and post-menopausal breast cancer. Remaining single, smoking and alcohol consumption were risk factors for pre-menopausal breast cancer while large height (> 159 cm), large body weight (>57 kg), large body mass index (BMI >26.5), passive smoking and frequent intake of ham and sausage were found to be risk factors for post-menopausal breast cancer. On the other hand, physical activity and frequent intake of carrots and chicken were inversely correlated with both pre- and post-menopausal breast cancer. A later age at menarche (>14 years old), irregular menstruation, parity, a large number of children, history of breast feeding, dietary control and frequent intake of bean curd, green vegetables and chicken were protective factors for pre-menopausal breast cancer, while frequent intake of fish and milk were inversely correlated with post-menopausal breast cancer. From their recent epidemiological study involving 1359 breast cancer cases and 23 163 control patients free of cancer[19], it was found that a large current BMI (>22.4) and a large increase in BMI (3.55) since the age of 20 were significant risk factors for post-menopausal breast cancer, while a large BMI (>24.1) at age 20 years old was a significant protective factor for post-menopausal breast cancer. From a recent epidemiological study of breast cancer conducted at the Osaka Medical Center for Cancer and Cardiovascular Diseases[20], high weight (>53 kg), large BMI (>25.1) and a family history of breast cancer were risk factors for post-menopausal breast cancer, while a large height (>159 cm) and high level of education were risk factors for pre-menopausal breast cancer. From these recent epidemiological studies in Japan, it is obvious that obesity after the age of 50 years is a clear and important risk factor for post-menopausal breast cancer.

Prevention of Breast Cancer

As breast cancer has been increasing in Japan and is predicted to increase further in the future, effective preventive measures, especially primary prevention should be undertaken. For primary prevention of breast cancer it is recommended that risk factors such as excess fat and calorie intake be avoided. It is also important to avoid obesity after the age of 50. For reproductive risk factors, it is desirable to avoid an older age at first pregnancy and delivery, but this may difficult for social reasons. To compensate for the difficulties in the primary prevention of breast cancer, secondary prevention of breast cancer such as breast cancer screening by mammography in combination with breast self-examination should be promoted.

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