[Environmental Health and Preventive Medicine 5, 155-159, January, 2001]

Original Article

Turning Points in Time Trends of Cancer Mortality in Japan: Premature Mortality is More Sensitive in the Progress of Cancer Prevention

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Abstract

The aims of this study were to demonstrate the trend of overall mortality rate and premature mortality rate for select types of cancer in Japan and to assess the utility as a target indicator. The age-adjusted mortality rate for the total population (overall mortality rate) and that for persons under 65 years of age (under 65 mortality rate) for stomach cancer, liver cancer and lung cancer from 1950 to 1997 in Japan were calculated. Moreover, the turning point year of the mortality trend was estimated using a regression model of the rate of annual increase in each mortality rate. As the results show, a decline in the under 65 mortality rate preceding a decline in the overall mortality rate was observed in stomach cancer and male liver cancer. Also, the under 65 mortality rate due to lung cancer seemed to begin to decline in recent years for males, while the overall mortality rate has been increasing. This study suggests that the premature mortality rate is a more sensitive indicator of the effectiveness of cancer prevention. Hence, because of not only the larger burden of premature deaths but also the sensitivity, premature mortality is considered to be suitable as a target indicator for cancer prevention strategies.

Key words: mortality rate, health policy, evaluation, target indicator, objective

Introduction

Recent health policies and health plans commonly set health targets and their objectives. Nationwide public health policy such Healthy People in the United States[1,2] and Health of the Nation and Our Healthier Nation in the United Kingdom[3,4] include target indicators and their objectives. Although the plan may be completed when this article is published, the Japanese Ministry of Health and Welfare is developing a new public health plan and strategies, named "Health Japan 21", which aims to reduce the incidence of non-communicable disease, especially lifestyle-related disease such as cancer and cardiovascular disease[5]. The plan is considered to include some kinds of health goals: target indicators and their objectives as well as other nationwide health plans.

As target indicators, premature mortality such as the mortality rate for persons under 65 years of age, is generally used [1,3,4]. Then a question arises: why is the premature mortality rate, rather than the overall mortality rate, suitable as a target indicator? One possible reason is in relation to the burden of disease. Burden of disease has been noticed from the viewpoint of health economics, and new health indicators related to the burden of disease such as Potential Years of Life Lost (PYLL) and Disability-Adjusted Life Years (DALY) have been established[6,7]. The burden of disease and death for a younger population is greater because the life expectancy is longer than that in the case of an older population. Hence, it is natural that premature death is viewed as a higher priority issue than elderly death.

However, if overall mortality and premature mortality show a similar trend, we don't need to adopt premature mortality particularly as a target indicator. The aims of this study were to demonstrate the time trend of age-adjusted mortality rate for selected types of cancer in Japan and to compare them. Moreover, using a regression model of the rate of annual increase in mortality rate, we estimated the turning point year when the increasing mortality rate began to decline. Also, considering these results, we tried to assess the utility of premature mortality rate in a health policy and in the evaluation of cancer prevention strategies.

Received Mar. 27 2000/Accepted Jul. 15 2000
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Methods

In this study, we focused on stomach cancer, liver cancer and lung cancer, because the mortality rate for stomach cancer and that for liver cancer have significantly changed, showing a decline rather than an increase in their time trend in the period for which data are available and lung cancer is now viewed as the highest priority issue in Japan.

The age-adjusted mortality rate for the total population (overall mortality rate) and the mortality rate for persons under 65 years of age (under 65 mortality rate) for stomach cancer, liver cancer, and lung cancer were calculated for the period from 1950 to 1997 with consideration given to sex and age-specific mortality[8, 9]. The mortality rate was adjusted according to the age distribution of the Japanese standard population in 1985[10]. The period for which liver cancer mortality was calculated was limited from 1968 to 1997, because of the availability of data on sex and age specific mortality.

The turning point year was estimated by regression analysis. The turning point year means the year when the increasing trend in mortality rate begins to decline. At first, the rate of annual increase in mortality was calculated. Next, a formula for the relationship between calendar year and the rate of increase was established as a linear regression model. As the turning point year, the year when the rate of increase was assumed to be zero was estimated by an extrapolation method using the computation formula. As well, turning point year was estimated in age-specific mortality for some kinds of cancers: stomach cancer, male liver cancer, and male lung cancer. The statistical analysis package SPSS 7.5/PC was used for the linear regression analysis.

Results

Figures 1 to 3 show the time trend of the overall age-adjusted mortality rate and under 65 mortality rate for stomach cancer, liver cancer and lung cancer, respectively. In the case of stomach cancer, the overall mortality rate was increasing in the 1950's, while the under 65 mortality rate plateaud or began to decrease. The overall mortality rate distinctly began to decrease after the 1960's.

Mortality due to liver cancer in males, both the overall mortality rate and the under 65 mortality rate, had been increasing dramatically since the late 1970's. As the method for death reporting and certification was changed in 1995, an artificial increase in the mortality rate was observed[11, 12]. Interestingly, the under 65 mortality began to decrease clearly in the 1990's, while the trend of the overall mortality rate was not conclusive. The mortality rate for liver cancer in females was lower and does not show a noticeable trend like that seen for males.

As shown in Fig. 3, the overall mortality rate for lung cancer in males had been increasing rapidly. Although not conclusive, the under 65 mortality rate for male was observed to plateau or slightly decline in the 1990's. For females, the mortality rate was lower than that for males, but it had been increasing steadily even in the 1990's.

As an example of the trend of the rate of annual increase in mortality rate, Fig. 4 shows the trend for stomach cancer in males. The formula for this trend obtained by regression analysis for the overall mortality rate and the under 65 mortality rate is 'rate of increase=326.4 - 0.17 × year', 'rate of increase=278.6 - 0.14 × year', respectively. The turning point year estimated using each of these formulas, when the rate of increase is zero, was 1962 and 1952, respectively.

The turning point year for each category of mortality was estimated as well, and the results are shown in Table 1. Regression analysis was performed using data for the period from 1975 to 1997 for stomach cancer, female liver cancer and female lung cancer. However, to make the coefficient of determination (R^2) larger, data for the periods 1950-1985, 1975-1997 and 1965-1997 for stomach cancer, male liver cancer and male lung cancer, respectively, were used. With respect to the types of cancer that showed a significant change in the trend from an increase to a decline, stomach cancer and male liver cancer, the turning point in the under 65 mortality rate was found to precede that of the overall mortality rate. The estimated turning point year for lung cancer in males was estimated to be 2000 for the overall mortality rate, and 1986 for the under 65 mortality rate. This finding reflects the fact that the under 65 mortality rate began to decrease in the late 1980's but the overall mortality rate had not yet begun to decrease.

For female liver cancer, the turning point year was estimated to be 1983 for overall mortality rate and 1996 for under 65 mortality rate. However, the coefficient of the formula was positive, which reflects the fact that there was a change in the mortality trend from a decline to an increase.

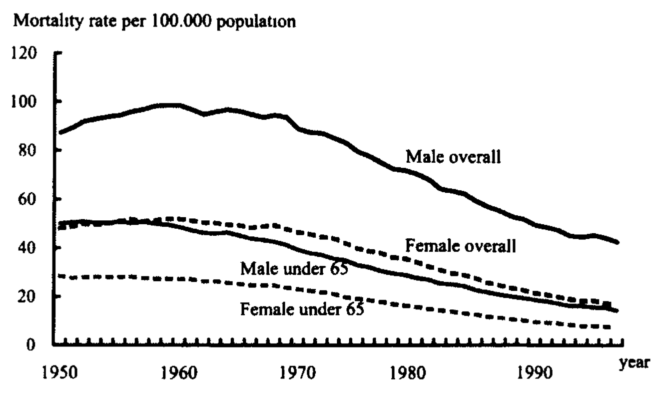

Fig. 1 The trend of age-adjusted mortality rate for stomach cancer in Japan. overall = age-adjusted mortality rate for the total population. under 65 = age-adjusted mortality rate for persons under 65 years of age.

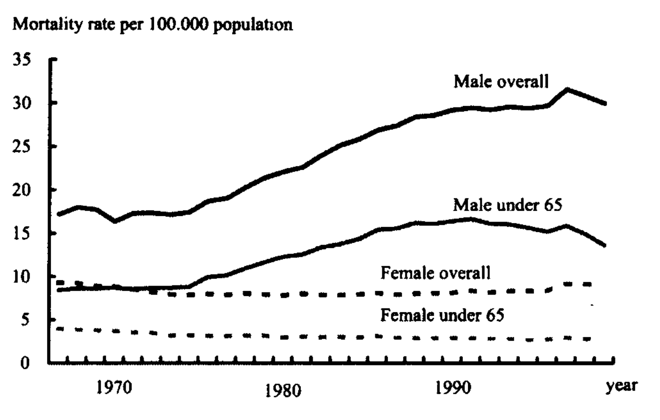

Fig. 2 The trend of age-adjusted mortality rate for liver cancer in Japan. overall = age-adjusted mortality rate for the total population. under 65 = age-adjusted mortality rate for persons under 65 years of age.

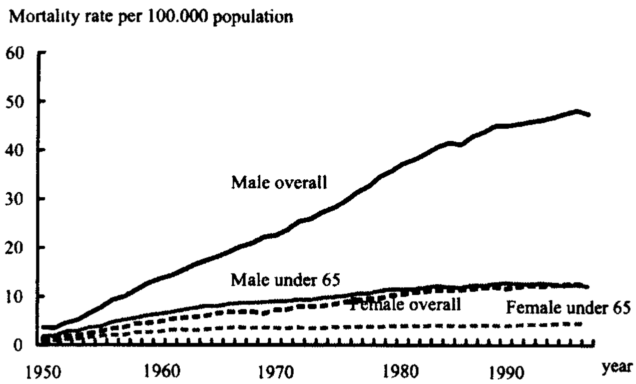

Fig. 3 The trend of age-adjusted mortality rate for lung cancer in Japan.
overall = age-adjusted mortality rate for the total population.
under 65 = age-adjusted mortality rate for persons under 65 years of age.

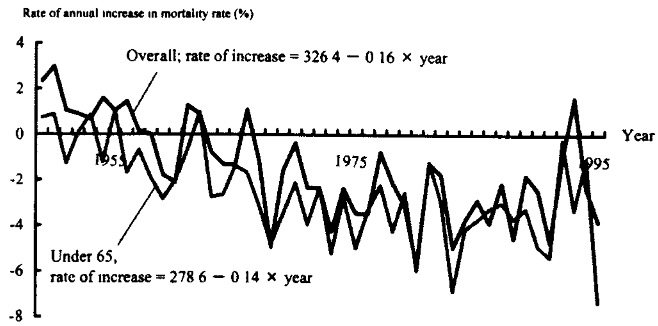

Fig. 4 Rate of increase in stomach cancer mortality rate for Japanese males.
overall = age-adjusted mortality rate for the total population.
under 65 = age-adjusted mortality rate for persons under 65 years of age.
The formula was established as a linear regression model for

Table 1 Turning point year as estimated by regression analysis of the rate of annual increase in mortality rate and calendar year.

Site	Sex	Mortality	A [a]	B [a]	R^2 [b]	Turning year [c]
Stomach	Male	Overall	326.4	-0.17	0.61	1961.5
		Under 65	278.6	-0.14	0.54	1952.3
	Female	Overall	351.4	-0.18	0.63	1959.4
		Under 65	297.4	-0.15	0.58	1952.9
Liver	Male	Overall	595.4	-0.30	0.45	1995.0
		Under 65	1189.7	-0.60	0.63	1990.0
	Female	Overall	-291.1	0.15	0.19	1983.4
		Under 65	-174.9	0.09	0.03	1996.3
Lung	Male	Overall	330.0	-0.17	0.58	1999.9
		Under 65	272.7	-0.14	0.35	1986.7
	Female	Overall	665.6	-0.33	0.41	1989.6
		Under 65	581.8	-0.29	0.16	1987.8

a. rate of annual increase=A + B × year
b: coefficient of determination
c: year when the rate of annual increase = 0

Table 2 Turning point year estimated by regression analysis of the rate of annual increase in age-specific mortality rate.

Site	Sex	age group							
		50-	55-	60-	65-	70-	75-	80-	85-
Stomach canser	Male	no value [a]	1948	1955	1958	1965	1970	1977	no value [a]
	(R^2)		(0.13)	(0.53)	(0.54)	(0.53)	(0.41)	(0.13)	
Stomach canser	Female	1952	1951	1949	1954	1962	1967	1973	no value [a]
	(R^2)	(0.18)	(0.25)	(0.34)	(0.38)	(0.48)	(0.32)	(0.17)	
Liver canser	Male	1989	1988	no value [a]	no value [a]	no value [a]	no value [a]	no value [a]	no value [a]
	(R^2)	(0.19)	(0.45)						
Lung canser	Male	no value [a]	no value [a]	1990	1994	1996	1998	2003	no value [a]
	(R^2)			(0.19)	(0.24)	(0.42)	(0.31)	(0.13)	

a) Turning point year is not estimated as the regression model is not sufficiently reliable (p>=0.05).
R^2. coefficient of determination

Moreover, the R^2 for the female mortality rate for liver cancer and the R^2 for the female under 65 mortality rate for lung cancer were so small that the regression model was not sufficiently reliable.

The estimated turning point year in the trend of age-specific mortality is shown in Table 2. The results demonstrate the tendency that the lower the age group was, the earlier the turning point year was. But the regression model in some age groups was not so sufficiently reliable and, therefore, the turning point year was not estimated. And R^2 in the regression model varied by age groups and sites of cancer.

Discussion

The results show that a decline in the under 65 mortality rate preceded a decline in the overall mortality rate for stomach cancer and male liver cancer in Japan. This study suggests that premature mortality rate is a more sensitive indicator of the effectiveness of cancer prevention than overall mortality rate. Therefore, we propose that premature mortality rate is more suitable as an indicator to be considered in setting health policy objectives. However, here we would like to discuss several points: (1) the consistency of these trends, (2) the reasons for these findings, (3) the suitability in the case of lung cancer, (4) age-specific mortality or age-adjusted mortality, and (5) the appropriate cut-off age for defining premature mortality.

To confirm that the premature mortality rate consistently begins to decline prior to the decline in the overall mortality rate, we should examine the trend in the case of other types of cancer. In Japan, there are some other types of cancer for which the mortality rate has been decreasing significantly in recent decades, e.g. esophageal cancer and uterine cancer[8, 9]. However, as both the overall mortality rate and the under 65 mortality rate for these types of cancer have been decreasing since 1950, we cannot compare the trends or estimate the turning point year.

Besides Japan, Bailar demonstrated a similar trend, that a decline in premature deaths was observed prior to a decline in overall deaths, in the United States. He first suggested the failure of cancer prevention in his country in the 1980's[13]. But, in the 1990's, he reported the effectiveness of cancer prevention, showing that there was a decline in premature mortality due to cancer, such as all malignant neoplasms and breast cancer, and he concluded that the cancer preventive strategies in the United States were successfully effective[14]. Therefore, because of the consistency in findings, comparing Japan and the United States, we conclude that the premature mortality rate is a more sensitive indicator of the effectiveness of cancer prevention strategies than overall mortality rate.

The second point of discussion is the reasons for this phenomenon. The context is probably very complex, considering the various types of cancer, the various kinds of risk factors, the preventive methods and age effects. However, we think there are at least two reasonable explanations. The first one is relation to the cohort effect. In the case of liver cancer, it is well known that the increase in mortality after the 1970's in Japan was due to the hepatitis virus infection, especially Hepatitis C virus infection[15, 16]. In Japan, the more elderly the population, the higher is the incidence of anti-HCV antigen seropositive individuals[15, 16]. As the high risk cohort has been passing out of the group aged under 65, the under 65 mortality has begun to decline. There has been no decrease in mortality in the older population yet because the high risk cohort is included in this age group. Second, risk reduction affects cancer morbidity for a younger population earlier than in the case of an older population. Because the older population is exposed to the risk factor longer, the effect is observed later. This hypothesis was established in the case of the relationship between smoking cessation and lung cancer[17].

The third point of discussion is connected with lung cancer. Prevention of lung cancer is one of the most important public health issues in Japan. Since male deaths due to lung cancer began to exceed deaths due to stomach cancer in 1992, lung cancer has been the leading cause of male death among all types of cancer. In general, the lung cancer mortality rate is mentioned to be increasing in Japan. However, our results show that at least the under 65 mortality began to decrease and Sobue has suggested that this reduction is among persons under 70 years of age[18].

It is well known that the most effective means of lung cancer prevention is a strategy to reduce the prevalence of smoking. The experience in England has suggested that there is a time lag between the reduction of the prevalence of smoking and the reduction of lung cancer mortality, which is a lag of almost 20-30 years[19]. In Japan, since the 1960's the incidence of smoking among males has been decreasing[20]. The observation that the mortality rate for male lung cancer began to decrease in the 1990's is consistent with the experience in England. Also, in the near future, the overall mortality rate for lung cancer is likely to begin to decrease.

However, we should not be optimistic. Unfortunately, the incidence of smoking among Japanese males is higher than that in other industrial countries. Also, in recent years, the incidence of smoking among young adult Japanese males has not been decreasing significantly and the incidence of smoking among young Japanese females is steadily increasing[21]. Hence, if this situation continues, lung cancer mortality rates for both sexes will probably not decline substantially.

Considering the fourth point, we are able to set the objectives in mortality for each age group. But, as this study shows, the reliability of regression models is lower in age-specific mortality rate than under 65 mortality rate and overall mortality rate. And for evaluation on preventive strategies, simple and limited target indicators are better. Therefore, aggregate mortality rate such age-adjusted mortality rate including under 65 mortality is more available as target indicators.

The last point of discussion is the cut-off age for defining premature mortality. PYLL is a major indicator of the burden of premature death. As the cut-off age, 60, 65 or 75 is used for the estimation of PYLL[22]. We do not have sufficient evidences to decide what age is most appropriate. However, we should consider the average age of death for each type of cancer when we define premature death due to cancer. The average age of death for lung cancer patients is higher than that for other types of cancer, and among cancer patients the lowest average age of death is that for breast cancer patients[23]. Therefore, it appears that we had better set the cut-off age for lung cancer higher, and that for breast cancer lower. The results of the turning point estimation in age-specific mortality show that the reliability of a regression model varies by age groups and sites of cancers. Although not conclusive, the tendency that age groups with high reliability are younger in case of stomach cancer than in lung cancer possibly supports our theory.

In conclusion, the present study demonstrates a difference in the time trends of overall age-adjusted mortality rate and under 65 mortality rate, and a decline in the under 65 mortality rate prior to overall mortality rate. The estimation of a turning point year in age-specific mortality supports the hypothesis that the decline of premature mortality precedes to that of overall mortality. These results suggest that premature mortality is a more sensitive indicator of the effectiveness of cancer prevention strategies than overall mortality. Among various measurements, the progress of cancer should be finally assessed on the basis of direct measurements such as mortality and incidence. Moreover, to assess whether there is a change from an increase to a decrease in cancer mortality rates, we propose that premature mortality is

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