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Prediction of the Gastric Cancer Mortality in 2000 in Japan

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Gastric cancer mortality in Japan in the year 2000 has been predicted from sex- and age-specific incidences and mortality trends and patient cure rates. The difference between the log-linear decrease in incidence and the log-quadratic decrease in mortality was considered to be the result of early diagnosis and treatment. Even on the assumption that 90% of patients could be cured in 2000, the number of deaths was estimated to be about 10,000. The decreasing incidence of cases brought about by birth cohort effects may contribute towards lowering the number of patients. The importance of health education in lowering the incidence of gastric cancer, by teaching people to keep up a sound life style, is discussed.

Key words: Gastric cancer — Mortality — Incidence — Prediction

To be able to predict the incidence of cancer and/or mortality is important from both administrative and scientific viewpoints. There are several mathematical methods for this purpose.[1–5] Extrapolation of the trend based upon the goodness-of-fit between past data and the mathematical model does not, however, necessarily predict the future trend.[6] This is because the predicted value should change as a result of the incidence of cancer being influenced by intervention or the mortality being lowered by a mass screening program, as well as by the development of treatment methods. In this regard, the predicted value needs to be supported by epidemiologic data, to show whether or not the value could be plausible. The rapidly decreasing gastric cancer mortality is often referred to as one of the successes in cancer prevention, early diagnosis and treatment.

The purpose of this paper is to analyze the trend in gastric cancer mortality up to the year 2000, predicting both the number of patients and the number of deaths. The plausibility of the predictions is examined by simulating the effects of treatment in 2000.

Materials and Methods

Numbers of deaths from stomach cancer according to sex and five-year age group were obtained from Vital Statistics in Japan, as well as from the relevant population. The data used for analysis were those classified into five-year periods from 1960 to 1985.[7] For calculating future numbers of deaths, the predicted population, published by the Institute of Population Problems in Japan,[8] was used. Numbers of gastric cancer patients were obtained from the cancer registry in Osaka[9] and A. Hanai (personal communication); other reports were also used as sources.[10–12] Basic data for calculation are listed in Table I.

The models used for the prediction were the linear and polynomial regression models with and without the log-transformation of dependent values. These calculations were carried out on a HITAC M-240H computer using the SAS program package (RSQUARE and GPLOT procedures). The method of least squares was used for fitting to the models. These models were evaluated in terms of r-square (R^2) and AIC (Akaike's information criteria).[13] AIC is a criterion for model selection and the formula is as follows: $AIC = -2\log(ML) + 2k$, where ML is the maximum likelihood of the model and k is the number of parameters. By using the AIC, both the goodness-of-fit and the conciseness of the model can be evaluated. The smaller the value of AIC, the better the validity of the model is supported.

Treatment effects for gastric cancer patients in different periods were obtained from the Gastric Cancer Study Group[14] and the 20th Annual Report of the National Cancer Center.[15]

Results

Trends in age-adjusted mortalities, adjusted to the population in 2000, from gastric cancer fitted well to the quadratic model; $R^2 = 0.991$ for males and $R^2 = 0.995$ for females. The predicted mortality in 2000 by this model became 19.2 per 100,000 in males and 0.70 in

Table I. Mortality and Incidence (per 100,000) Adjusted to the Population in 2000

		1960	1965	1970	1975	1980	1985
Mortality	Males	119.2	116.4	107.3	94.7	82.7	72.1
	Females	73.9	71.1	67.6	58.3	50.7	41.6
		1966–68	1969–71	1972–74	1975–77	1978–80	1981–83
Incidence	Males	168.2	154.8	144.1	134.8	128.0	128.4
	Females	95.8	88.3	84.4	76.8	72.5	67.8

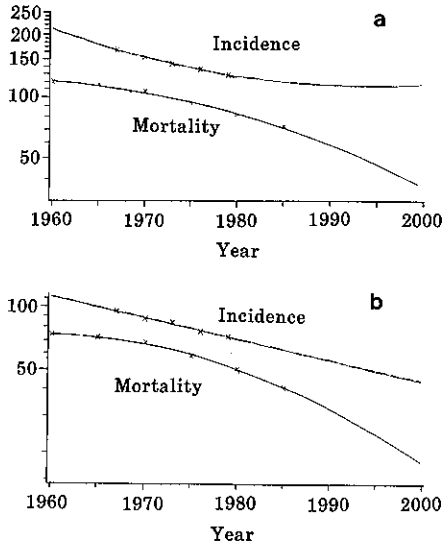

Fig. 1. Trends in gastric cancer incidence and mortality in males (a) and females (b), calculated using the log-quadratic model. Difference between incidence and mortality becomes larger toward 2000. The vertical axis shows the standardized number of patients per 100,000 population in 2000.

females. Furthermore, the log-quadratic model showed better fitting; $R^2=0.996$ for males and $R^2=0.998$ for females. The extrapolated mortality for 2000 was 37.3 per 100,000 in males and 17.9 in females (Figs. 1 a and b). The log-linear model did not yield a good fit on this occasion; $R^2=0.959$ for males and 0.934 for females. The AIC values of the log-linear model were -35.6 for males and -31.4 for females, while those of the log-quadratic model were -47.5 and -49.5, respectively. Extrapolated plausible mortality for 2000 was 37.3 and 17.9, respectively (Table II).

Changes in the incidences of gastric cancer, obtained from the Osaka Cancer Registry, for the years 1966–68, 1969–71, 1972–74, 1975–77 and 1978–80, yielded the following fitting parameters: log-quadratic model, $R^2=1.000$, AIC $=-62.9$ for males and $R^2=0.991$, AIC $=-40.9$ for females. Applying the log-linear model also gave a good fit; $R^2=0.993$, AIC $=-44.0$ for males and $R^2=0.991$, AIC $=-42.9$ for females. The log-linear model fitted slightly better in the case of females. The estimated incidences, calculated by using the fitted equations were 114.8 per 100,000 for males and 44.4 for females. Summarizing the above data, the trend of mortality is decreasing in a log-quadratic mode in both males and females, and the incidence is log-linearly decreasing in females and log-quadratically decreasing in males, although the latter seems to be reaching a plateau. Differences between the incidence and mortality became larger toward 2000 in both males and females, as predicted by the best-fitting models. Estimations of the number of gastric cancer patients and deaths and death rate in 2000 are summarized in Table II.

The five-year survival rate of gastric cancer patients treated between 1963 and 1966 in 103 hospitals was only 33.6%. This value was similar to that in the National Cancer Center Hospital in the same period. At that time, 28.1% of the patients were inoperable, and only 26.0% of the patients operated upon were Stage I curable cancer cases (Fig. 2a). The five-year survival rate between 1969 and 1973 rose to 43.6% in 56 major hospitals, probably due to a decrease in the number of inoperable cases and an increase in the number of patients at Stage I. Treatment results in the National Cancer Center during the period 1971–1985 show a five-year sur-

Table II. Estimated Population, Gastric Cancer Patients and Death in 2000

	Population ($\times 10^5$)	Incidence ($/10^5$)	No. of patients	Mortality ($/10^5$)	No. of patients	Death rate[a] (%)
Males	65,129	114.8	74,768	37.3	24,293	32.5
Females	64,990	44.4	28,856	17.9	11,633	40.6
Total	130,119	79.6	103,624	27.6	35,926	34.7

a) Death rate was calculated as mortality/incidence $\times$ 100.

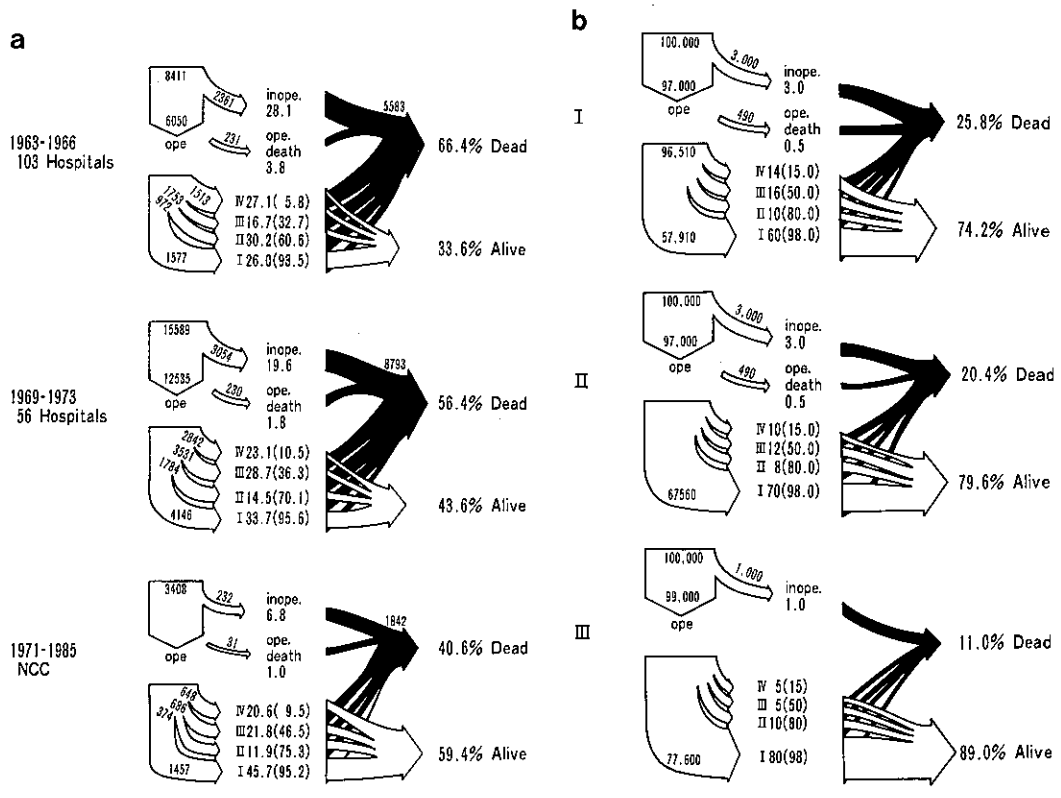

Fig. 2. (a) Flow of patients and effect of past treatment. The increased proportion of five-year survivors is mainly due to increased rates of early gastric cancer (Stage I). Black arrows indicate flow of patients to death, and white arrows to survival. I–IV, Stages I–IV, respectively. Numbers in arrows indicate actual numbers of patients; those after stages indicate proportions of patients; and those in parentheses indicate five-year survival rates. (b) Hypothetical flow of patients and effect of treatment in 2000. Top figure (I), possibly attainable; bottom (III), ideal but too optimistic; middle (II), arbitrary situation between the two.

vival rate of 59.4%. The inoperable cases decreased to 6.8% and patients at Stage I increased to 45.7%. It is noteworthy that the five-year survival rates for patients at Stages I and IV remained at almost the same values throughout these periods, although patients at Stages II and III in the National Cancer Center showed a slight improvement.

The state of treatment considered for 2000 is shown in Fig. 2b. Three different scenarios

were arbitrarily selected based on discussions with clinicians who are experts on gastric cancer treatment. As it is thought that the number of gastric cancer patients in 2000 will be about 103,600, the starting number was set at 100,000. In the case illustrated in Fig. 2b (top), inoperable cases would account for 3.0% and patients at Stage I 60%; the mortality rate would be 25.8%, and this value would be slightly better than that arising from the data shown in Table II, in which death occurred in 32.5% of incident cases in males, 40.6% in females and 34.7% for both. If the incidence of Stage I patients could be increased to 70%, the increase in the five-year survival rate would still be only 5% (Fig. 2b, middle). The most optimistic estimate of treatment effects would yield an 89% five-year survival rate, but in that event, 80% of patients should be detected at Stage I (Fig. 2b, bottom).

Discussion

To be able to predict the trends in cancer incidence and mortality is important both for scientific research and the public health service.[6] Mathematical models are usually used, but the goodness-of-fit does not necessarily predict the actual number of future patients. Log-quadratic models have been preferred empirically for predicting future trends,[11, 12] although some authors have preferred log-linear models.[16] In the present study, R^2 and AIC showed a good fit of the log-quadratic model for mortality of both males and females and for incidence in males, but the log-linear model was better for incidence in females. The discrepancy between males and females in incidence could be coincidental, because only a few points were available for estimation of incidence. The continuous decrease in gastric cancer mortality rate shown in the log-quadratic form greatly exceeded the decrease in gastric cancer incidence. This difference has usually been considered to have resulted from mass-screening and treatment development.

Analysis of treatment effects for three different periods in the past revealed an increased proportion of operable cases, mostly due to early detection, since the proportion of patients at Stage I had steadily increased. The National Cancer Center, however, is considered as being one of the most advanced hospitals in Japan, so that such results could be favorably biased. The five-year survival rates for Stages I and IV were similar for the 56 hospitals used in the 1969–1973 study and for the National Cancer Center Hospital in 1971–1985, however, so that the increased five-year survival rate was, on the whole, considered as being due to the increased number of cases at Stage I. Should the advanced inoperable cases decrease by half and Stage I gastric cancer occupy 60% of operable cases, the estimated five-year survival rate would rise to 74% (Fig. 2b). Such a scenario is plausible. The number of patients (incident cases) in 2000 can be considered to be 100,000–120,000[11, 12] or 100,000 in the present study and the number of deaths from stomach cancer 30,000. The proportion of deaths among the patients would be approximately one-third for both males and females, making the treatment effect situation consistent with simulation I in Fig. 2b. To achieve a greater decrease in mortality, earlier detection would be necessary, unless effective revolutionary treatment methods were to be developed. If inoperable cases could be reduced to less than 1% of patients and if it were possible to find 80% of patients at Stage I, the estimated five-year survival rate would reach approximately 90%; however, the number of deaths from gastric cancer would remain at around 10,000.

Is it possible to reduce the number of deaths from gastric cancer to below 10,000? In the US today the number of gastric cancer deaths is about 5,000 after an adjustment to the Japanese population. This number is almost the same as the number of deaths in today's Japan from tuberculosis, which had been the leading cause of death several decades ago. It is well known that gastric cancer is influenced by environmental risk factors. In the United States, the decline in gastric cancer is considered to be associated in some way with the growing use of electric refrigerators, which has changed the methods of food storage, preparation and handling.[17–19] Tominaga[20] suggested the importance of a reduction in salt intake, since food nitrates can be transformed to nitrites, which may be carcinogenic in the stomach.

The altered dietary habits of Japanese immigrants in Hawaii decreased the rate of gastric cancer there.[21] Such a phenomenon is to be observed in other ethnic investigations.[22] The age-specific stomach cancer mortality rate in Japan has decreased in birth cohorts through a declining number of associates. This declining tendency of the risk among birth cohorts born after 1900 has been clearly observed (Hanai and Fujimoto, personal communication). Since a person's life style is often established in the early stages of life, risk factors closely related to the established life style could be interpreted as cohort factors. It is important to recognize that the existence of cohort effects does not imply that preventive activities for high risk birth cohorts are hopeless. Several risk factors for stomach cancer have been identified to date on the basis of descriptive and/or analytical epidemiology.[23] Improvements in socio-economic status, dietary pattern, medical technology, etc., are considered to have contributed to the lowered incidence of gastric cancer. In this respect, a further continuous decrease in the incidence of gastric cancer can be expected. Should it become halved by 2000, the 10% death rate for 50,000 patients would yield 5,000 deaths from gastric cancer.

The simulation of gastric cancer in this study indicated that even ideally advanced therapy would not be able to reduce the gastric cancer mortality in Japan by 2000 to the level in the United States today, but it should be possible to reduce its incidence by altering dietary habits and life style.[23,24] In this respect, an educational approach towards a better life style would appear to be most important and effective.

In the present study, histologic differences have not been considered. The majority of gastric cancer cases in Japan are tubular adenocarcinoma, however suggesting that macroscopic considerations have not greatly influenced the outcome of this study. Histologic type in relation to age effect will be dealt with in a separate paper.

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