RESEARCH COMMUNICATION

Long-Term Prediction of Female Breast Cancer Mortality in Korea

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Abstract

Not only the incidence but also the mortality of female breast cancer has been steadily increasing in Korea since the 1980s. Epidemiologic evidence on changes in lifestyle and risk factors related with breast cancer, and data from migrant studies strongly suggest that breast cancer might further increase. In order to estimate the long-term trend in mortality of breast cancer in Korean women, we analyzed age-specific mortality rates for breast cancer over the past 20 years, and made a projection up to 2020 using a linear regression model with the Poisson distribution. The age-adjusted mortality rates for breast cancer per 100,000 persons were 2.84 in 1983, 4.91 in 1993, and 6.26 in 2003. The predicted expected age-adjusted mortality rates for breast cancer are 6.51 for 2005, 7.37 for 2010, 8.22 for 2015, and 9.07 for 2020, with an estimated annual increment of breast cancer mortality of 0.1704. Accordingly, 1,564 women in 2005 and 3,087 in 2020 will be expected to die of breast cancer in Korea. Compared with the rate in 1983, this indicates a more than 3-fold increase by 2020. On the basis of our results, female breast cancer in Korea will linearly increase for the forseeable future if the trend over the past 20 years continues.

Key Words: Breast cancer - mortality - forecasting - Korea - linear models - trends

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Introduction

Breast cancer is one of the most frequently diagnosed cancers in women and its incidence has increased over the past twenty years. Global differences in breast cancer rates show lower incidences in less developed regions compared with more developed regions (Ferlay et al., 2004), but the increasing trend in age-adjusted rates is becoming similar across the world (Kelsey et al., 1993, Cancer Statistics in Japan 2003). Korea is one country where the mortality rates for breast cancer are still low (Parkin et al., 1997, World Health Statistics, 1998), but the incidence rate of female breast cancer has been increasing steadily in a linear pattern since the 1980s (Korea National Statistical Office, Yoo et al., 1992). Breast cancer now ranks fifth as a cause of death in women and first in terms of cancer incidence in 2002 (Korea Central Cancer Registry, 2003).

It has long been proposed that breast cancer might be closely related with female ovarian hormones (Pike et al., 1993). Recent large-scale, multi-center case-control analyses pointed to the importance of lifetime exposure to estrogen and diet in Korean women, compatible with the estrogen-augmented-by-progesterone-hypothesis. Furthermore change in dietary habits, nutritional status, and reproductive behaviors has occurred in young Korean women, which may be in favor of further increase in breast cancer in Korea (Park et al., 1998, Yoo et at., 2002).

Both estimating of lifetime risk and verifying the high-risk groups are essential to develop a control strategy against breast cancer. The present study was designed to predict the mortality of female breast cancer by 2020, using mortality data over the past 20 years in Korea.

Materials and Methods

Mortality Data

Data on the annual number of deaths due to female breast cancer from 1983 to 2003 were obtained from the Korean National Statistical Office. Age-specific mortality rates were calculated by dividing ages into groups as follows: 0-14,

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15-34, 35-39,40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-75 and 75 and over. The respective crude mortality rates for breast cancer were calculated using the number of females in the population as a denominator. Breast cancer cases were defined as code 174 (malignant neoplasm of female breast) according to the International Classification of Diseases, 9th Revision (ICD-9), and as code C50 (malignant neoplasm of breast) in the 10th Revision (ICD-10). Age-adjusted mortality rates were calculated with respect to the female population of 2005 as the standard (Table 1).

Prediction Models

Predictions were made by extrapolating the breast cancer mortality trend during1983 -2003 to the next 20 years. Age-specific mortality rates were linearly regressed on calendar year and also 5-year-age groups, under the assumption of a Poisson random error (Dyba et al., 2000). The linear form, rather than logarithm link, controlled against explosively increasing predictions (Dyba et al., 2000, Yang et al, 2004). The following predictive model, as an age-adjusted linear model, has been used for predicting breast cancer mortality:

$$E(M_t) = \alpha + \beta t \quad (1)$$

where t is a numerical value for period.

Age-adjusted mortality rates can potentially mask differences between age-specific trends, which can produce biased results (Dyba et al., 2000). Hence, each age group was separately modeled. To consider different patterns of the annual changes between the younger and the older age group from Figure 1, different slope parameters were assumed:

$$E(M_{it}) = \alpha_i + \beta_i t \quad (2)$$

where i = 1,2,...,10, α_i is the estimates of age-specific rates for baseline year (1983), and β_i is the estimates of annual change in each age group. The predicted expected mortality rates and the 95% confidence intervals were also calculated. The group of age 0-14 was excluded from the prediction because of the low mortality rate.

The standard population for age-adjusted death rate was the population of 2005, estimated by the National Statistical Office database. Total numbers of deaths were predicted by summing up the age-specific deaths for each corresponding year. The log-likelihood ratio statistic (deviance) was used to test the goodness of the fitted models. All the statistical analyses were performed using SAS 8.0.

Results

Table 1 shows the crude and age-specific mortality rates for breast cancer observed during 1983-2003 in Korea. From the Table 1, both crude and age-adjusted mortality rates are increasing. The former is more rapidly increasing than the latter along with growth of Korean female population. The pattern of the mortality rates by age is changing with the calendar year; showing sharply increasing tendency up to the 50s, and then slightly decreasing during the early observed years, while it is again increasing in the age of 70s in the late observed years.

Table 2 provides the parameter estimates from the models for age-specific and age-adjusted mortality rates. The age-specific annual increment of breast cancer mortality in each age group was represented by βs The age over 75 was the most rapidly increasing with time, while there were no significant changes in the age under 45. The age-adjusted mortality rates have been significantly changing, annual gaining of 0.1704 per 100,000 persons (p=0.02).

The predicted expected age-specific and age-adjusted mortality rates and their 95% confidence intervals are shown in Table 3. The predicted expected age-adjusted mortality rates, standardized by 2005 Korean female population are 6.51, 7.37, 8.22 and 9.07 per 100,000 for the year of 2005, 2010, 2015 and 2020, respectively. Compared with the rate in 1983, which is 2.84 per 100,000, it is increased more than 3 times in 2020. The predicted expected crude rates are 6.50, 8.25, 10.20 and 12.21. As the predicted year increases, the 95% confidence interval goes wider, implying lower precision. The maximum width of the confidence intervals, about 13 per 100,000, happens to the age 50-54 in 2020. It suggests that the predicted mortality rates in Table 3 must be fairly precise provided that the models used in prediction will hold true in the future. However, the last two lower bounds in the age of 15-34 could not be properly estimated because of the negative values of estimates.

Table 4 shows the observed and the expected number of deaths. Since only one case of breast cancer death was found in the age of 0-14 during the past 20 years, the predicted total cancer cases would not be affected by exclusion of the age group from the prediction model. The predicted numbers of deaths are 1,564, 2,034, 2,556 and 3,087 persons for the year of 2005, 2010, 2015 and 2020, respectively. Hence, female breast cancer deaths in 2020 will have a gain 100% over the year of 2005. Figure 1 and 2 display the age-specific and age-adjusted mortality rates of breast cancer. Also, these models were well fitted because the goodness-of-fit tests using deviance did not reject the hypothesis that the model is well fitted (p> 0.5).

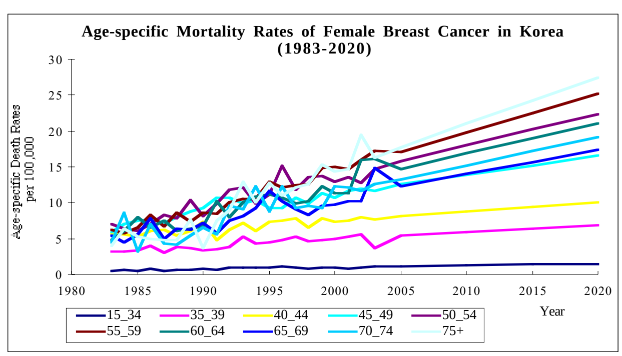

Figure 1. The Observed (1983-2003) and Predicted (2005-2020) Age-specific Death Rates (per 100,000) of Female Breast Cancer in Korea

Table 1. Crude and Age-specific Mortality Rates for Female Breast Cancer per 100,000 in Korea (1983-2002)

Age	Year										
	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993
0-14	0	0	0	0	0	0	0	0	0	0	0
15-34	0.52	0.62	0.52	0.73	0.53	0.64	0.66	0.78	0.61	0.89	0.95
35-39	3.25	3.22	3.31	3.92	3.00	3.86	3.62	3.31	3.45	3.88	5.19
40-44	5.82	5.51	5.20	6.12	6.24	5.46	6.12	7.36	4.82	6.27	7.17
45-49	5.93	7.04	7.46	7.59	7.26	7.93	8.79	9.19	10.66	10.72	9.94
50-54	7.06	6.31	6.07	7.05	8.29	7.83	10.43	8.14	9.89	11.87	12.08
55-59	6.19	5.68	6.48	8.33	6.66	8.67	7.34	8.59	8.47	10.04	10.46
60-64	4.87	6.11	8.02	6.57	7.55	6.02	6.45	6.63	10.28	8.03	10.11
65-69	5.43	4.55	5.63	7.76	4.93	6.38	6.21	7.23	5.74	7.58	8.21
70-74	4.43	8.64	3.23	6.96	4.28	4.14	5.45	6.58	5.58	9.62	9.03
75+	3.97	6.36	5.19	4.98	4.79	4.85	7.68	3.72	7.54	8.98	12.99
Crude rates	1.86	2.04	2.03	2.40	2.21	2.38	2.66	2.73	2.87	3.40	3.81
Adjusted rates[1]	2.84	3.11	3.02	3.50	3.18	3.34	3.71	3.70	3.88	4.48	4.91

Age	Year									
	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
0-14	0	0	0	0	0.02	0	0	0	0	0
15-34	1.03	0.88	1.04	0.90	0.83	0.94	1.0	0.78	0.96	1.18
35-40	4.33	4.46	4.87	5.20	4.56	4.80	4.97	5.33	5.51	3.69
44-49	6.13	7.29	7.55	7.88	6.49	7.86	7.34	7.55	7.96	7.65
50-54	10.34	9.30	9.32	10.62	9.82	11.33	10.71	11.58	11.94	11.70
55-54	9.92	11.19	15.17	11.80	13.50	13.66	12.97	13.58	12.74	14.69
55-59	10.57	12.95	12.13	12.39	12.68	14.86	14.92	14.65	15.99	17.28
60-64	10.87	11.25	10.72	9.94	10.28	12.30	11.4	11.28	15.93	16.08
65-69	9.23	11.71	10.14	9.17	8.36	9.51	9.79	10.18	10.21	14.85
70-74	12.28	8.73	12.22	9.20	9.64	9.19	12.31	12.13	11.61	12.60
75+	10.09	12.82	10.98	12.19	12.54	15.36	14.32	14.68	19.43	16.21
Crude rates	3.74	4.04	4.35	4.28	4.24	4.88	4.93	5.10	5.72	5.97
Adjusted rates[1]	4.73	5.02	5.27	5.09	4.96	5.59	5.52	5.61	6.13	6.26

[1] Age-adjusted mortality rates standardized by female population of 2005 in Korea.

Discussion

This study suggests that the female breast cancer mortality in Korea would further increase, especially, for older women. Compared with 3.97 per 100,000 in 1983, the increment of the mortality rates is alarming. Note that in Table 2, the rate increases most rapidly in the age over 75 and then the age of from 55 to 59. Specifically, the expected mortality rate in the group of age over 75 is 27.49 in 2020. As shown in Table 3, the age-adjusted mortality rates will be 9.07, which are resulted from applying population in 2005, and the predicted crude rates in 2020 will be 12.21. We may explain that the 26% of crude mortality rates in 2020 can be explained by growth of population in Korea.

Figure 2 shows that a log-linear model may result in over-prediction, even though its deviance was not significantly different from the model with identity link. Therefore we used an identity link to control explosively increasing predictions (Hakulinen et al., 1986).

Figure 3 shows the past and the future age-specific mortality trends by age in Korea. In 1980s, the curves are bell-shaped, which have the maximum mortality in the age of mid-fifties. The shape of this curve in Korea is consistent with other studies (Ahn et al., 1994, Park et al., 1998). However, the trend has been changed from the early 1990s. It reached the peak in the age of 50s and slightly decreased in 1980s, but it increases again from the age of 70 from the 1990s. Korea is entering quickly to aging society so that increasing rate of breast cancer death rate would be related to the longevity. Also, it could be an emerging sign of a birth cohort effect, just like in Japan (Minami et al., 2003).

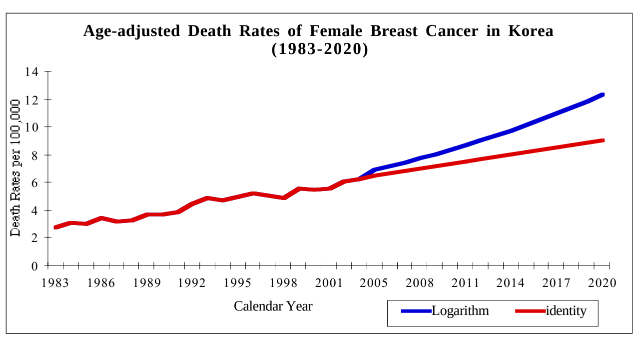

Figure 2. The Observed and Predicted Age-adjusted Death Rates of Female Breast Cancer in Korea (1983-2020)

Table 2. Parameter Estimates from the Following Prediction Models; $E(M_{it}) = \alpha_i + \beta_i t$, for Age-specific Mortality Rates, $E(M_t) = \alpha + \beta t$ for Age-adjusted Mortality

Model	Parameter	Age	Estimates	P-value
Age-specific Rates	$\alpha_i s$	15-34	0.5493	
		35-39	3.1697	
		40-44	5.4279	
		45-49	6.8706	
		50-54	6.3549	
		55-59	5.3934	
		60-64	5.2726	
		65-69	4.8296	
		70-74	4.4907	
		75+	3.4992	
	$\beta_i s$	15-34	0.0259	0.4222
		35-39	0.1009	0.1701
		40-44	0.1229	0.1828
		45-49	0.2615	0.0192
		50-54	0.4323	0.0002
		55-59	0.5336	<.0001
		60-64	0.4284	<.0001
		65-69	0.3400	0.0006
		70-74	0.3979	<.0001
		75+	0.6485	<.0001
Age-adjusted Rates	α		2.7652	0.0004
	β		0.1704	0.0217

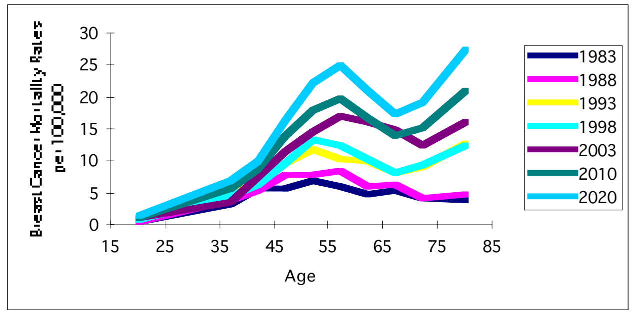

Figure 3. The Age-specific Mortality Curves for Observed and Predicted Years

Age-specific incidence curves suggest that breast cancer as a hormone dependent cancer arises from a multistage process. Unlike the unopposed estrogen hypothesis for endometrial cancer, both ovarian hormones are considered to play critical roles in breast cancer risk. All of the key epidemiologic findings can be explained by an "estrogen-augmented-by-progesterone hypothesis" for breast cancer. In spite of the lower incidence, there is no difference in the breast cancer risk factors between Korea and Western countries (Yoo et al., 1995, Yoo et al., 2002, Lipworth et al., 2000, Lee et al., 2003). Mainly reproductive factors as early menarche, late menopause, late full-term pregnancy and never-having had a breast-fed child, have been defined as women at higher risk. Among the environmental factors, although it is controversial yet, diet, physical activity, obesity, alcohol drinking, cigarette smoking, ionizing radiation, pesticides, and electromagnetic fields have been recognized as established or potential risk factors (Park et al., 1998). It has been hypothesized that international variation in breast cancer incidence might be partially related to variation in such factors as body weight, some aspect of diet, hormonal levels, and reproductive factors (Parkin et al., 1997). Of the factors, postmenopausal obesity has been revealed as an important risk factor for breast cancer in Korea (Yoo et al., 2001). Also, obesity is closely related to the early menarche, and to late menopause. Improvements in nutritional status also brought an improvement in the physical condition of the young girls, i.e., height, weight, age at menarche.

The other biological factor that can be used to explain this difference is the level of female sex hormones, which were found to be much lower than those found in American women. Genetic polymorphisms in the potential roles in the metabolism of hormones, dietary carcinogens and tobacco

Table 3. Predicted Mortality Rates for Female Breast Cancer per 100,000 in Korea (2005-2020)

AGE	YEAR 2005 Mortality rates	2005 95% CI	2010 Mortality rates	2010 95% CI	2015 Mortality rates	2015 95% CI	2020 Mortality rates	2020 95% CI
15-34	1.12	0.20, 2.04	1.25	0.04, 2.46	1.38	-0, 2.90	1.51	-0, 3.33
35-39	5.39	3.34, 7.44	5.89	3.17, 8.61	6.40	2.99, 9.81	6.90	2.79, 11.01
40_44	8.13	5.59, 10.67	8.75	5.37, 12.13	9.36	5.11, 13.61	9.98	4.85, 15.10
45_49	12.62	9.50, 15.75	13.93	9.78, 18.08	15.24	10.04, 20.43	16.54	10.28, 22.81
50_54	15.87	12.51, 19.23	18.03	13.60, 22.45	20.19	14.67, 25.71	22.35	15.72, 28.98
55_59	17.13	13.79, 20.47	19.80	15.44, 24.17	22.47	17.06, 27.88	25.14	18.66, 31.62
60-64	14.70	11.55, 17.84	16.84	12.72, 20.96	18.98	13.86, 24.10	21.12	14.99, 27.26
65_69	12.31	9.40, 15.22	14.01	10.18, 17.83	15.71	10.95, 20.47	17.41	11.70, 23.12
70-74	13.24	10.29, 16.19	15.23	11.38, 19.09	17.22	12.44, 22.01	19.21	13.48, 24.94
75+	17.77	14.56, 20.98	21.01	16.87, 25.15	24.25	19.16, 29.35	27.49	21.43, 33.55
Adjusted rates[1]	6.51	4.37, 8.66	7.37	4.54, 10.19	8.22	4.69, 11.75	9.07	4.83, 13.31
Crude rates[2]		6.50		8.25		10.20		12.21

[1] Age-adjusted mortality rates were standardized by female population of 2005 in Korea.
[2] Crude rates were calculated by using the predicted total breast cancer deaths from Table4 and expected female Korean population.

Table 4. Observed and Predicted Number of Deaths due to Female Breast Cancer Estimated by the Poisson Regression Model in Korea (1985-2020)

Age	Calendar Year							
	Number of breast cancer deaths observed				Number of breast cancer deaths predicted[1]			
	1985	1990	1995	2000	2005	2010	2015	2020
0-14	0	0	0	0	-	-	-	-
15-34	40	65	72	79	81	84	88	88
35-39	41	49	89	104	111	124	118	126
40-44	57	89	107	145	169	179	196	183
45-49	78	98	111	154	248	287	311	345
50-54	53	83	117	152	227	351	414	453
55-59	45	73	129	153	198	279	433	510
60-64	45	44	92	110	147	190	262	399
65-69	23	38	73	77	114	134	171	233
70-74	10	24	41	70	96	131	154	198
75+	19	18	74	106	173	275	409	552
Total	411	581	905	1,150	1,564	2,034	2,556	3,087

[1]Number of deaths due to breast cancer was predicted by multiplying death rates and predicted female population in Korea based on the national statistics from the National Statistical Office.

carcinogens have been investigated to figure out the inherited differences in capacity to metabolize environmental carcinogens in Korea (Kim et al., 2002). Nested case-control studies on genetic susceptibility within the cohort using biological materials bank will give us further insight into both the etiology and the prevention of this malignancy.

On the basis of our results, female breast cancer in Korea has been increasing, especially in the older age groups. Therefore, risk prediction by risk factor stochastic model, and the risk management through screening, lifestyle change, surgical or chemoprevention for women at high risk should be pursued for the prevention of this malignancy. The predicted deaths in this study can also be used as a baseline data to assess the effect of those policies, because the prediction was made under the assumption that the trend in the past 20 years would continue into the future (Reissigova et al., 1994).

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