RESEARCH ARTICLE

Past Trends and Future Estimation of Annual Breast Cancer Incidence in Osaka, Japan

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Abstract

Background: Although the breast cancer incidence rate in Japan is lower than in western countries, the age-specific rates have markedly increased in recent years, along with the problems of declining birth rate and an aging population. Materials and Methods: We examined past trends of age-specific breast cancer incidence using data from the Osaka Cancer Registry from 1976 to 2010, and estimated future trends until 2025 based on the changes observed and population dynamics using a log linear regression model. Results: The age-specific breast cancer incidence rate has increased consistently from the 1970s, and the rates have caught up with those of Japanese-Americans in the US. Assuming the increasing tendency of age-specific breast cancer incidence to be constant, the average annual incidence of breast cancer will increase 1.7-fold from 2006-2010 to 2021-2025. Furthermore, the number of patients aged 80 years should increase 3.4-fold. Conclusions: The medical demand for breast cancer care in Japan may increase explosively in the future, particularly among the elderly. We need to prepare for such a future increase in demand for care, although careful monitoring is needed to confirm these results.

Keywords: Breast cancer incidence - future trends - age-specific incidence - Japanese - Japanese-Americans

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Introduction

Although the age adjusted breast cancer incidence rate in Japan, 51.5 per 100,000 person-years, is still much lower than in Western countries: e.g., 92.9 in the USA, 79.8 in Canada and 95.0 in the UK (International Agency for Research on Cancer, 2012; Katanoda et al., 2015), rates have been rapidly increasing in recent years and 13,148 Japanese women died of breast cancer in 2013 (International Agency for Research on Cancer, 2013).

Furthermore, there is marked age-specific variation of breast cancer incidence worldwide. In western countries, the rate increases rapidly before the menopause, and increases gradually afterward. On the other hand, in low incidence countries including Japan, the increase after the menopause is low or even negative (Bray et al., 2004; Matsuno et al., 2007). The peak of age-specific breast cancer incidence in Japan was 45-54 years, while the peak age in western countries is 70-79. Recently, the rates of breast cancer in women aged 40 years or under in Japan have become close to those in western countries. However, there remain some difference between the Japanese and western country rates for women in their 50s and over (World Health Organization, 2014). Since the Japanese life-style became westernized in the post World War II period (Egusa et al.2004), age-specific breast cancer incidence rates of Japanese have been getting close to those of Japanese-Americans.

In recent decades, population dynamics of a declining birth rate and an aging population have been observed in Japan. Baby booms occurred in 1947-1949 and 1971-1974 and the number of births has continued to decline since the second boom. As a result, the population is aging rapidly. The proportion of the total population aged 65 years or over in Japan is the highest in the world: 23.1% in 2010 (United Nations, 2015). By 2030, one in three people will be aged 65 years or over, and one in five people will be aged 75 years or over (Muramatsu et al., 2011). Thus, absolute numbers and the trends of breast cancer incidence in Japan would be greatly influenced by the changes in population dynamics and age-specific incidence rates.

In the present study, we examined past trends of age-specific breast cancer incidence in Osaka, and estimated the future volume of breast cancer cases until 2025, based on the changes in age-specific incidence rate and population dynamics.

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Materials and Methods

Initial examination for the age-specific breast cancer incidence rate

The Osaka Cancer Registry (OCR), which was established in 1962, is a population-based cancer registry that covers the Osaka prefecture (population: 8.9 million [2010 census]). Using OCR data regarding invasive breast cancer incidence (International Classification of Diseases, 10th revision; C50) among women who were diagnosed between 1976 and 2010, we examined breast cancer incidence by age (5 year intervals), and age-specific breast cancer incidence rates according to the incident year. The incident years were divided into 5-year time periods from 1976–1980 to 2006–2010. The population data by age group in Osaka prefecture were obtained from the Population Census. Cases with missing age data were excluded from our analysis.

Estimation of future volume

In order to estimate future volume, we obtained data on the assumed future age-specific population in Osaka from the website of the National Institute of Population and Social Security Research (National Institute of Population and Social Security Research, 2015).

Using 1976–2010 data, the age-specific breast cancer incidence rates in 2011-2015, 2016-2020 and 2021-2025 were estimated on the basis of the following two scenarios.

<u>Scenario A</u>: The age-specific breast cancer incidence rates in Osaka in 2011-2015, 2016-2020, and 2021-2025 were calculated by log linear regression model (Yang L., 2004).

<u>Scenario B</u>: Similarly to scenario A, the future rates were calculated by log-linear regression model. However, use of a constantly increasing tendency may cause an overestimation of the future rates. In order to avoid such overestimation, we assumed the Japanese-Americans data as the upper limit of the rates in scenario B. When the calculated future age-specific incidence rates in Osaka were higher than the rate of Japanese-Americans (the latest available average data), we applied the rates of Japanese-Americans as the predicted future age-specific incidence in Osaka.

The data for the age-specific incidence rate of Japanese-Americans were obtained from the website of Cancer Incidence in Five Continents: Los Angeles (2003-2007), San Francisco (1998-2003) and Hawaii (2003-2007) (World Health Organization, 2014). We adopted the average rate of these three areas as representative of Japanese-America data.

The statistical software package IBM SPSS Statistics 23.0 for Windows (IBM Japan Inc., Tokyo, Japan) and was used for data analysis.

Results

A total of 70,139 cases of female invasive breast cancer were identified from the OCR between 1976 and 2010. Of these, 187 cases were excluded from the analysis because of missing age data, leaving a total of 70,132 to be used in this study.

Table 1 shows past trends and future estimates in the age-specific breast cancer incidence rate in Osaka and among Japanese-Americans. For past trends, the rate for women aged 30 years or over has been increasing generally. The peak occurred in the pre-menopause group, i.e. 45-54 year olds. For the 49 years and under group, the rates were close to those among Japanese-Americans. For women aged 50 years or over, despite increasing trends, the rates in Osaka were still lower than those of Japanese-Americans.

For the future estimates, the rates in Osaka for women aged 35-39 years, 40-44 years and 45-49 years in 2016-2020 overtook those for Japanese-Americans. For those aged 50 years or over in 2021-2025, there were still gaps between Osaka and the Japanese-Americans. Figure 1 shows the age distribution of the female population in Osaka in 2010 and 2025. Detailed data are shown in Table 2. It shows rapid population aging and bimodal distribution caused by the two baby booms. In 2021-2025,

Table 1. Trends in the Age-Specific Incidence Rates per 100,000 Person-Years

	Past trends							Future Estimation						
	Incident year							Incident year			Japanese-Americans			
Age	1976-1980	1981-1985	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025	L. A.*	S. F.**	Hawaii*	Average
-24	0.1	0.2	0.2	0.2	0.2	0.3	0.1	0.2	0.2	0.2				
25-29	3.6	4.7	3.9	3.8	4.5	4.3	4.5	4.6	4.7	4.8	5.0	10.8	3.2	6.3
30-34	9.6	14.0	13.7	12.3	15.9	15.3	19.1	19.6	21.4	23.3	43.4	26.3	23.7	31.1
35-39	22.0	29.1	36.8	36.9	40.8	41.6	43.9	53.0	58.8	65.2	49.3	47.8	67.1	54.7
40-44	38.8	48.8	58.9	67.2	77.0	81.4	101.1	117.3	136.0	157.8	127.9	81.8	146.6	118.8
45-49	55.0	67.7	75.9	86.3	117.7	123.8	149.9	177.7	209.8	247.8	214.8	156.0	182.8	184.5
50-54	56.1	61.5	71.6	76.6	96.5	125.9	136.4	158.7	185.7	217.3	285.8	193.7	240.2	239.9
55-59	50.6	62.9	69.6	73.2	96.7	107.2	153.7	161.9	191.7	227.0	303.7	322.8	279.1	301.9
60-64	51.5	64.1	77.5	76.9	87.7	109.7	141.0	151.4	176.0	204.6	351.7	457.6	302.6	370.6
65-69	54.4	57.9	73.5	77.8	89.8	106.2	148.7	155.0	181.6	212.7	197.9	264.9	338.8	267.2
70-74	48.8	62.2	72.6	73.8	95.3	97.9	125.9	140.3	161.9	187.0	292.0	260.2	424.8	325.7
75-79	43.4	53.5	65.6	68.1	91.3	102.7	126.9	148.3	176.4	209.8	310.7	323.4	353.8	329.3
80-84	43.2	57.2	51.3	77.2	74.4	94.1	130.3	138.2	163.3	193.0	411.8	295.4	393.6	366.9
85-	19.4	49.8	51.7	53.4	71.1	74.8	107.9	134.9	168.9	211.3	286.4	189.4	328.7	268.2

** 2003-2007, obtained from Cancer Incidence in Five continents Volume I to X; ** 1998-2003, obtained from Cancer Incidence in Five continents Volume I to X; L.A.= Los Angeles, S.F=San Fransisco the first and second baby boomers will be aged 75-79 years and 45-49 years, respectively.

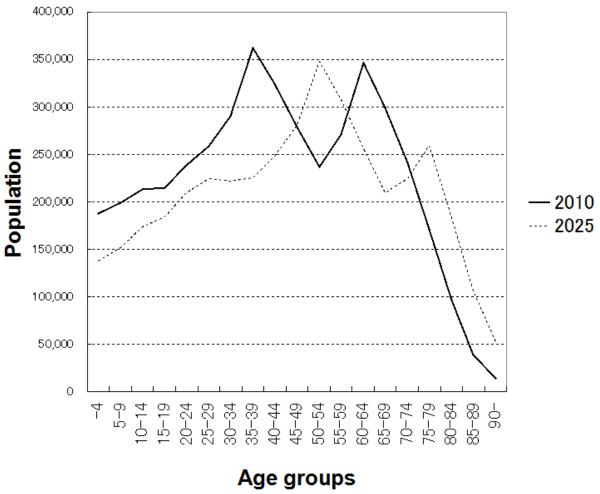

Figure 1. Age Distribution of Female Population in Osaka in 2010 and 2025

Figure 2 shows past trends and future estimates of average annual breast cancer incidence in Osaka in scenarios A and B. Detailed data are shown in Table 3. For past trends, the number for all age groups has been

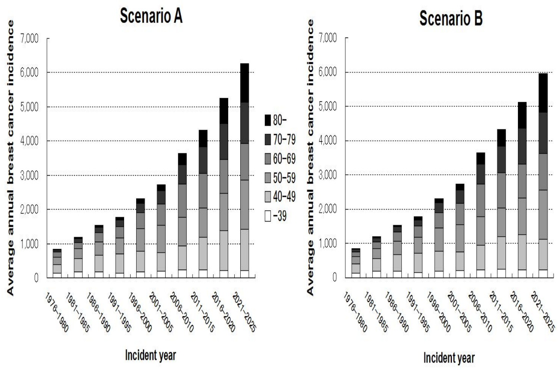

Figure 2. Past Trends and Future Estimates of Average Annual Breast Cancer Incidence in Osaka in Scenarios A and B

Table 2. Trends and Future Estimates of Average Women Population According to Age Group

Age	Year 1976-1980	1981-1985	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010	2011-2015*	2016-2020*	2021-2025*	2026-2030*
-24	1,620,091	1,589,526	1,518,257	1,395,037	1,239,859	1,113,114	1,032,943	982,824	924,397	852,874	780,956
25-29	376,312	297,133	297,627	337,964	373,174	334,675	277,830	246,460	224,957	220,016	210,434
30-34	413,738	359,257	283,947	283,461	322,739	358,484	326,358	275,856	242,445	222,320	217,715
35-39	361,783	396,656	344,705	271,988	272,973	312,342	350,558	324,030	271,627	239,203	219,533
40-44	311,076	351,514	386,352	336,090	265,722	267,719	309,193	350,678	320,832	269,154	237,132
45-49	266,873	304,399	344,699	380,296	330,556	261,621	265,369	309,843	348,071	318,515	267,370
50-54	216,350	259,359	296,951	337,822	371,591	323,751	258,719	265,693	306,919	344,752	315,643
55-59	174,839	208,484	250,147	288,673	328,199	362,315	317,755	257,736	262,112	302,738	340,214
60-64	148,753	166,973	198,736	240,189	278,282	318,864	353,529	314,315	252,921	257,357	297,435
65-69	127,630	139,989	157,402	188,990	228,957	267,712	308,393	347,900	307,393	247,555	252,144
70-74	94,727	115,787	128,076	145,885	176,076	216,375	255,105	299,213	335,487	297,008	239,723
75-79	60,798	79,583	99,480	112,241	130,358	160,949	198,749	239,430	279,702	315,248	280,206
80-84	30,993	43,745	59,639	77,698	90,914	110,087	138,290	176,270	212,130	249,410	283,814
85-	14,422	22,092	34,033	51,728	76,548	105,635	136,580	182,417	241,235	305,788	375,025

* Obtained from National Institute of Population and Social Security Research

Table 3. Trends and Future Estimates in the Average Annual Breast Cancer Incidence According to age Group

	Past Trend					Future estimates (Scenario A)				
	Incident year					Incident year				
Age	1976-1980	1981-1985	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025
-39	135	183	180	152	182	202	230	239	224	220
40-49	268	378	489	554	594	541	710	962	1,167	1,214
50-59	210	291	387	470	676	794	841	839	1,073	1,436
60-69	146	188	270	332	450	633	957	1,015	1,003	1,053
70-79	73	115	158	184	287	376	573	775	1,037	1,217
80-	16	36	48	88	122	182	328	490	754	1,127
Total	847	1,190	1,531	1,779	2,310	2,729	3,640	4,319	5,257	6,267
	Past Trend					Future estimates (Scenario B)				
	Incident year					Incident year				
Age	1976-1980	1981-1985	1986-1990	1991-1995	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025
-39	135	183	180	152	182	202	230	239	213	195
40-49	268	378	489	554	594	541	710	962	1,023	907
50-59	210	291	387	470	676	794	841	839	1,073	1,436
60-69	146	188	270	332	450	633	957	1,015	1,003	1,053
70-79	73	115	158	184	287	376	573	775	1,037	1,217
80-	16	36	48	88	122	182	328	490	754	1,127
Total	847	1,190	1,531	1,779	2,310	2,729	3,640	4,319	5,102	5,936

increasing generally. The increasing tendency after 1996-2000 was noticeable for women aged 60 years or over. For future estimates, the average annual breast cancer incidence increased 1.7-fold: from 3,640 in 2006-2010 to 6,267 in 2021-2025 for scenario A, and 1.6-fold: to 5,936 in 2021-2025 for scenario B. A difference in average annual breast cancer incidence between scenario A and B was observed in the number of women aged 40 years after 2016-2020.

In scenario A, the proportion of women aged 40 years or under in 2021-2025 was 19% (1,214/6,267), compared with 15% (907/5,936) in scenario B. A declining tendency in women aged 40 years from 2021-2025 was apparent in scenario B. In both scenarios, the proportion of women aged 80 years or over increased rapidly: from 9% (328/3,640) in 2006-2010 to 18% (1,127/6,267) in 2021-2025 for scenario A, and to 19% (1,127/5,936) in 2021-2025 for scenario B.

Discussion

In the present study, we revealed the past tendency of increasing breast cancer incidence, and estimated future trends using OCR data.

The age-specific breast cancer incidence rate had been close to that of western countries. Possible factors that have contributed to the rapid increase in breast cancer incidence in Japan include: reproductive factors (Kawai et al., 2010; Kawai et al., 2012), smoking (Nagata et al., 2006), obesity (Suzuki et al., 2011), and height (Green et al., 2011). A combination of these factors is probably responsible for the change in age-specific breast cancer incidence. In particular, as mentioned above, reproductive factors (age at first birth, breastfeeding, parity) have changed noticeably.

Population dynamics in Japan have two key characteristics: an aging population and two baby booms. The number of births peaked in 1949 (269.7 per 10,000) and in 1973 (209.2 per 10,000) and the number of births since the second baby boom has decreased consistently. The total fertility rate in Japan peaked in 1947 (4.32) and decreased thereafter. In the last two decades, the rate has remained at the same level, around 1.3. As a result, bimodal distribution, rapid population aging, and declining birth rate are now occurring. Under such circumstances, breast cancer incidence and the age structure of breast cancer patients will change remarkably.

In the present study, the volume of elderly breast cancer cases (aged 80 years or over) was estimated to increase 3.4 fold in 2021-2025. Although breast cancer cases among the very elderly (85 years or over) were relatively rare (4%) in 2006-2010, these would become common (10%) in 2021-2025. On the other hand, the proportion of pre-menopause cases would decrease. When the upper-limit of age-specific breast cancer incidence rates was set as Japanese-Americans data, the proportion of breast cancer women aged less than 50 years was estimated to decrease from 26% (940 /3,640) to 19% (1,127/5,936). Even when the rates increase at the present pace, the proportion would decrease to 22% (1,434/6,267).

Although the findings of the present study were limited to Osaka, the age-specific incidence rates from 1976 to 2010 in Osaka prefecture were very similar to those in all Japan (Matsuda et al., 2013). When the findings of the present study were generalized to the whole of Japan, several points could be considered.

First, the demand for medical care of breast cancer in Japan may increase explosively in the future, particularly for the elderly. When the number of invasive breast cancer cases increases, the demands for medical care of breast cancer will also increase. The demands probably do not have linear regression with the number of invasive breast cancer cases because there are a relatively high number of cases of non-invasive breast cancer. In the present study, non-invasive breast cancer (International Classification of Diseases, 10th revision; D05) cases were not included. However, 329 non-invasive breast cancer cases per year were diagnosed and registered with OCR in 2006-2010, while the number of invasive breast cancer cases was 3,640. The estimated number of non-invasive breast cancer cases for all Japan in 2010 is 7,970, while the number of invasive breast cancer cases is 68,071 (Matsuda et al., 2013). In Japan, although the screening rate using mammography was only 36.4% in 2011 (Organization for Economic Co-operation and Development, 2013), the number of non-invasive breast cancer cases reached approximately one-tenth of the number for invasive breast cancer. Cancer screening cannot avoid false-positives and over-diagnosis (Welch et al., 2010). Therefore, a wider spread of screening would bring more demands for medical care of breast cancer: not only treatment for non-invasive breast cancer, but also further clinical examination after screening. Furthermore, the amount of work per one invasive breast cancer case has increased noticeably. Many kinds of chemotherapy and endocrine therapy have been developed in recent decades, and development is continuing now (Early Breast Cancer Trialists' Collaborative Group, 2005; Ahmed S, 2015). As a result, the prognosis for breast cancer has improved. However, this also means the demand for medical care of breast cancer has become much greater. The increase in demand for medical care of breast cancer may be much greater than the increase in invasive breast cancer incidence.

Secondly, the age distribution of breast cancer patients in Japan may change remarkably. Since mammography alone is an inadequate tool for breast cancer screening for women in their 40s (Smith et al., 2004; Smart et al., 1995), a randomized controlled trial for a screening program using mammography plus ultrasonography for Japanese women in their 40s is ongoing (Ohuchi et al., 2011; Ishida et al., 2014). However, the importance of breast cancer control for these women may be small because the annual breast cancer incidence among those aged under 50 years in 2021-2025 might be relatively low.

The present study has some limitations. First, there are missing cases in the OCR. The proportion of death certificates only, which is often regarded as an index of completeness, was approximately 10-15% and registration has been stable in the OCR for the last two decades (Curado et al., 2007). Therefore, breast cancer incidence as a whole might be underestimated. Secondly, the future increase in age-specific breast cancer incidence in Osaka is uncertain. In order to estimate the future volume, we had to use the assumption that the incidence rate would increase at the present pace (scenario A) and not overtake the latest available Japanese-American data (scenario B). However, the situation of mammography is different between these countries; screening rates using mammography in 2011 were 36.4% in Japan, compared with 80.4% in the US (Organization for Economic Co-operation and Development, 2013). Further deliberation would depend on whether the Japanese data would reach the Japanese-American level with or without extending breast cancer screening. Furthermore, there may be a birth cohort effect in the trends in Japanese breast cancer incidence rate. In previous studies, the birth cohort effect for breast cancer incidence in Osaka gradually increased and peaked with the 1950s birth cohort, and then slightly decreased (Minami et al, 2004; Ito et al, 2011). Since the birth cohort effect was not considered, our estimate for women aged 50 years or under after 2011-2016 might be overestimated. Third, because we used data from the Osaka cancer registry, we need to interpret the findings with limited generalizability to the whole of Japan. The proportion of aging population and change in incidence rate vary across prefectures. In addition, distributions of risk factors which affect change in incidence rate also differ.

In conclusion, under the assumption that age-specific breast cancer incidence increases at the present pace, the average annual breast cancer incidence in Osaka would increase 1.7-fold from 2006-2010 until 2021-2025. The number for women aged 80 years or over would increase 3.4-fold. If these findings were generalized to the whole of Japan, the demands of breast cancer care in Japan might change remarkably. We need to prepare for future trends for breast cancer care, although careful monitoring is needed to confirm these findings.

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