Significant Difference in the Trends of Female Breast Cancer Incidence Between Taiwanese and Caucasian Americans: Implications from Age-Period-Cohort Analysis

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Abstract

Female invasive breast cancer (FIBC) in Taiwan is characterized by a striking recent increase of incidence and a relatively young median age (45-49 years) at diagnosis. The Westernization of lifestyle that is increasingly affecting younger generations of Taiwanese may have an important impact on this change. We compared epidemiologic data on FIBC in Taiwanese obtained from the Taiwan Cancer Registry with data for Caucasian Americans obtained from the database of the Surveillance, Epidemiology, and End Results Program for the period from 1980 to 1999. Age-specific incidence rates of FIBC were plotted by calendar year at diagnosis and by birth cohort for both populations. The individual effects of time period and birth cohort on the incidence trends of FIBC in both populations were evaluated using the age-period-cohort analysis. The incidence rate of FIBC was continuously increased in Taiwanese throughout the past 2 decades, whereas the increase of incidence was slowing down in Caucasian Americans. The incidence rates in Taiwanese women born after the 1960s were approaching that of Caucasian Americans. The age-period-cohort analysis showed a much stronger birth cohort effect on the incidence trend of FIBC in Taiwanese than in Caucasian Americans. This strong birth cohort effect corresponded to the Westernization of lifestyle in Taiwan since 1960. These findings indicate that a continued shift in the incidence and age distribution pattern of FIBC in Taiwanese toward that of Caucasian Americans should be anticipated. (Cancer Epidemiol Biomarkers Prev 2005;14(8):1986–90)

Introduction

The incidence of breast cancer varies widely in different geographic areas (1). Lifestyle and other environmental factors have been implicated in the variation in breast cancer incidence. A ''Westernized'' lifestyle, usually referred to as the combination of early menarche, decreased parity, and delayed childbearing, a diet rich in saturated fat, and a sedentary life pattern, is associated with the increased incidence of breast cancer (2, 3).

Prior to the 1980s, Taiwan was categorized as having a low incidence of breast cancer (4). However, the age-adjusted incidence of female invasive breast cancer (FIBC) in Taiwan has increased dramatically from 11.72 per 100,000 women in 1980 to 38.78 per 100,000 women in 1999 (adjusted by U.S. standard population in 2000). This increasing trend is similar to that of most Asian countries which have experienced a similar trend of Westernization of lifestyle and environment in the last few decades (5-8). The median age at diagnosis of breast cancer in Taiwan (45-49 years) is lower than that of Western countries (70-74 years). It is not clear whether the differences in incidence and age distribution of FIBC between Taiwanese and Western populations results from ethnical or genetic susceptibility or from environmental risk factors.

The age-period-cohort (APC) analysis is commonly used by epidemiologists to analyze trends of disease incidence and mortality (9, 10). It is designed to estimate, in addition to the effect of patients' age, the individual effects of time period at diagnosis and patients' birth cohort, which are usually overlooked in cross-sectional studies. The age effect usually reflects physiologic differences affecting susceptibility to the disease among different age groups. The time period effect usually reflects factors that affect all age groups equally at a given period of time, such as introduction of screening programs or new diagnostic techniques, a carcinogen that acts in the late-stage of tumorigenesis, or an improvement in the completeness of data registration. The birth cohort effect, on the other hand, indicates factors that affect unequally among different birth cohorts and require prolonged time to manifest their effects on tumorigenesis. A typical example is change of lifestyle, which is usually determined early in adult life and acts on the early stages of tumorigenesis. Analysis of birth cohort pattern is therefore important in understanding the implications of lifestyle in the trend of breast cancer incidence (11, 12).

To explore the different trends of FIBC incidence between Taiwanese and the Western populations and possible contributing factors, the current study compared epidemiologic data of FIBC from 1980 to 1999 between Taiwanese and Caucasian Americans. The APC model was applied to analyze the relative effects of time period and birth cohort on the trend of FIBC incidence in both populations.

Materials and Methods

Sources of Data. Epidemiologic data (incidence rates, patient number, and population size) on FIBC (International

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Note: Y-C. Shen, C-J. Chang, and C. Hsu contributed equally to this work.

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Classification of Diseases, 9th revision code 174) from 1980 to 1999 for Taiwanese were obtained from the Taiwan Cancer Registry (http://www.doh.gov.tw/). The Taiwan Cancer Registry was founded in 1979 by the Department of Health of Taiwan. It is a population-based cancer registry with the collection of information on cancer patients newly diagnosed in hospitals with 50 or more beds throughout the country and was estimated to encompass about 80% of all breast cancer cases in Taiwan (13). Data from the Taiwan Cancer Registry have been used to show the decrease in incidence of childhood hepatocellular carcinoma after hepatitis B vaccination for children in Taiwan (14). Epidemiologic data on FIBC during the same period for Caucasian Americans were adopted from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute of the U.S. (http://seer.cancer.gov/) with the following selection criteria: SEER registry, nine SEER registries; site, breast; race, non-Hispanic White; and sex, female. Data from subjects with age younger than 30 years in both populations were omitted because of the low case number. Data from patients age 85 or older were also excluded because of the very low case number in Taiwanese and difficulty in specifying their corresponding birth cohorts. Eligible data were primarily categorized into 11 5-year age groups (from 30-34 to 80-84 years) and 4 5-year time period groups (from 1980-1984 to 1995-1999), implying 14 overlapping 9-year birth cohort groups (from 1896-1904 to 1961-1969).

Age-specific incidences of FIBC during 1980 to 1999 were plotted by calendar year at diagnosis and by birth cohort for both populations. A simple log-linear model was used to estimate the average annual percentage change of incidence to confirm the analytic observations through visual inspection, based on the assumption of a constant annual growth rate in incidence throughout the whole period (10). Tests of the variables in this model were two-sided and a P value of <0.05 was considered as statistically significant. A second-order polynomial model including a quadratic term was also constructed to test for a possible quadratic effect (10).

The APC analysis was fitted based on two assumptions. First, the number of cases over a time period followed Poisson's distribution. Second, the incidence rate was a multiplicative function of age, time period, and birth cohort. Thus, the logarithm of the incidence rate was expressed as a linear combination of the effects of age, time period, and birth cohort as follows:

$$\ln(\lambda_{ijk}) = \ln\frac{\mu_{ijk}}{n_{ijk}} = \rho + \alpha_i + \beta_j + \gamma_k + e_{ijk}$$

where λ_{ijk}, μ_{ijk}, and n_{ijk} denote the incidence rate, the mean number of patients, and the number of individuals, respectively, in the i^{th} age group (i = 1, 2,..., I), j^{th} time period group (j = 1, 2,..., J) and k^{th} birth cohort group ($k = I - i + j$). α_i, β_j, and γ_k represent the effects of the i^{th} age group, j^{th} time period, and the k^{th} birth cohort group, respectively; ρ is the intercept term and e^{ijk} is the random error term.

Owing to the linear dependence between age, time period, and birth cohort (age = time period − birth cohort), the individual estimate of the effect of the three main factors cannot be uniquely identified. Therefore, the regression coefficients of the first and last periods were constrained as zero to provide first-order relative risk estimates of cohort, and vice versa (15). The estimates of relative risk, reflecting the individual effect of time period and birth cohort, were generated by the maximum likelihood method. The time period 1985 to 1989 and the birth cohort 1926 to 1934 were used as reference groups for estimates of relative risk.

The deviance, degree of freedom, and adjusted R^2 were used to measure the goodness-of-fit of each model. A smaller deviance and degree of freedom imply a better fit of a given model. Adjusted R^2, which shows the variability that can be explained by factors other than age, was also used as a measure of the fit of different models compared with the age model. A level of adjusted R^2 closer to 1 means a better fit. F test was used to test for significance of differences in deviance between the full APC model and the two-factor models. The analyses were conducted with SAS software (version 8.1).

Results

Trends of FIBC Incidence in Taiwanese and Caucasian Americans by Calendar Year at Diagnosis. From 1980 to 1999, 37,740 FIBC cases aged between 30 and 84 years were diagnosed in Taiwan, and 241,154 for Caucasian Americans in nine SEER registries. The age-specific incidence rates of FIBC for each 5-year period from 1980 through 1999 in both populations are shown as Fig. 1. Although the incidence rates of FIBC for Caucasian Americans steadily increased with age and plateaued at around 75 to 84 years, the peak incidence of FIBC for Taiwanese was between 45 and 59 years. The incidence rates were higher in Caucasian Americans than in Taiwanese for all age groups, particularly for older groups. However, in the youngest group (30-34 years), the incidence rate in Taiwanese has been approaching that in Caucasian Americans during 1980 to 1999 (from 10.40 of 100,000 in 1980-1984 to 22.38 of 100,000 in 1995-1999 for Taiwanese; compared with 24.86 of 100,000 in 1995-1999 for Caucasian Americans). In fact, the incidence rates for women aged 30 to 34 years in both populations in 1999 were very similar (24.91 of 100,000 for Taiwanese and 24.20 of 100,000 for Caucasian Americans).

Trends of FIBC Incidence in Taiwanese and Caucasian Americans by Birth Cohort. The age-specific incidences of FIBC of representative birth cohorts in Taiwanese and Caucasian Americans are shown as Fig. 2. For Caucasian women, the increase in FIBC incidence with increasing age seemed similar between earlier (e.g., 1906-1914 and 1916-1924) and later (e.g., 1946-1954 and 1956-1964) cohorts. For Taiwanese women, by contrast, the increase in FIBC incidence with increasing age was slower in earlier cohorts and became steeper in later cohorts. With regard to the later cohort group (1956-1964), the trends of FIBC incidence with increasing age became similar between the two populations.

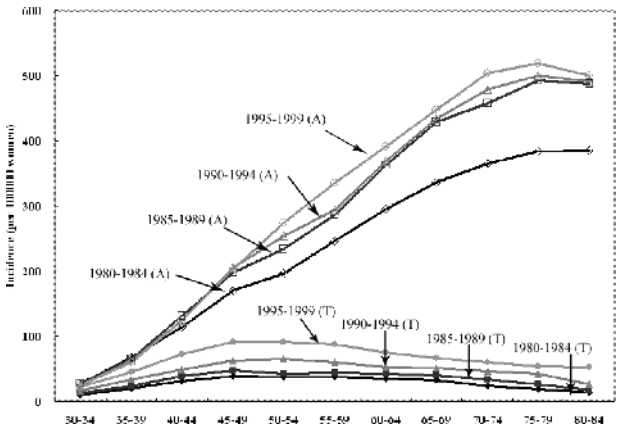

Figure 1. Age-specific incidence rates of FIBC in Taiwanese and Caucasian Americans by calendar year at diagnosis (T, Taiwanese; A, Caucasian American).

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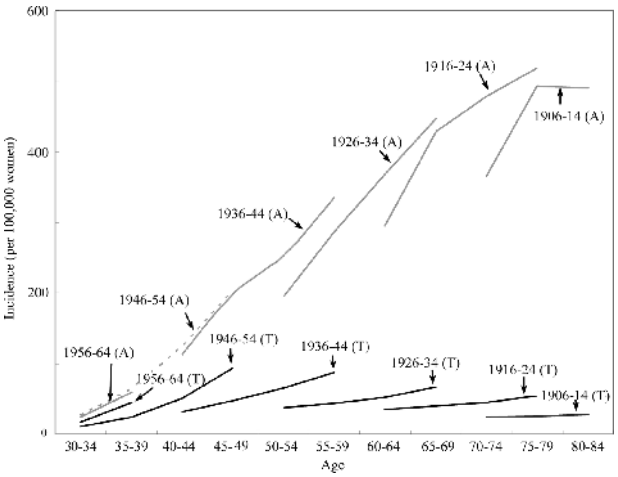

Figure 2. Age-specific incidence rates of FIBC in Taiwanese and Caucasian Americans by birth cohort (T, Taiwanese; A, Caucasian American).

For women born in the last cohort group of 1961 to 1969 years (data not shown in Fig. 2), the incidence rate of breast cancer at age of 30 to 34 years in Taiwanese (23.03 of 100,000) was quite close to that of Caucasian Americans (24.08 of 100,000).

The Secular Trend of FIBC Incidence in Taiwanese and Caucasian Americans by the Simple Log-Linear Model. The average annual percentage change of FIBC incidence in Taiwanese from 1980 to 1999 is shown in Table 1. The annual increase of the overall incidence (30-84 years) throughout the past 2 decades was much higher for Taiwanese (6.68%), compared with that for Caucasian Americans (1.25%). In Taiwanese, the increasing trend was noted in all age groups. A positive quadratic trend term, which indicates a continuing trend of incidence increase, was significant in age groups of 40 to 44, 50 to 54, and 50 to 64 years. Contrarily, the incidence increase slowed down for almost all age groups of Caucasian Americans.

APC Analysis on FIBC Incidence in Taiwanese and Caucasian Americans. Table 2 summarizes the statistics comparing goodness-of-fit for different models. In either Taiwanese or Caucasian Americans, the full APC model provided a much better fit than any two-factor models because of a significant difference in deviance between each two-factor model and the full APC model ($P < 0.05$). Thus, the full APC model was adopted to generate estimates of relative risk, reflecting the individual effects of time period and birth cohort.

Relative risks and their 95% confidence intervals for time periods and birth cohorts are shown in Fig. 3. The birth cohort effect was much stronger in Taiwanese than in Caucasian Americans. For example, the relative risk for Taiwanese women born in 1961 to 1969 was 7.29, whereas it was 1.37 for Caucasian Americans born in the same period, compared with that of women born from 1926 to 1934. The period effect was also positive in Taiwanese, whereas it was negligible in Caucasian Americans, particularly for those diagnosed as having breast cancer after 1985.

Discussion

In this study, we showed that the incidence of FIBC in Taiwanese has rapidly increased throughout the past 20 years, in contrast to the much slower incidence increase in Caucasian Americans during the same period. Noticeably, the incidence rates of FIBC among Taiwanese women born after the 1960s have been approaching those of Caucasian Americans. It may suggest that younger generations of both populations share common environmental exposure, which has a greater impact upon the pathogenesis of FIBC than ethnical or genetic susceptibility. Furthermore, the APC analysis showed a stronger birth cohort effect on the incidence trend of FIBC in Taiwanese than in Caucasian Americans. The strong birth cohort effect in Taiwanese indicates that changes in environmental exposure between women born in earlier and later cohorts plays an important role in the pathogenesis of FIBC.

The major environmental differences between younger and older generations in Taiwan seemed to be the increasing Westernization of lifestyle. Taiwan has become increasingly industrialized since the 1960s. Therefore, women born after the 1960s have been exposed to more high-calorie and high-fat diets in their childhood and generally had increased body mass index than women from previous generations. Increased height and body mass indexes were reported as positive predictors of early menarche (16), and are well-confirmed risk factors of breast cancer as well as early menarche (17-21). Nulliparity and lower parity have been associated with an increased risk for breast cancer in

Table 1. Age-specific annual percentage change of FIBC incidence in Taiwanese and Caucasian Americans during 1980 to 1999

Age (y)	Taiwanese				Caucasian Americans			
	Linear model		Model with a quadratic trend term		Linear model		Model with a quadratic trend term	
	Age-specific annual percentage change (%)	*P*	Sign of the second order term	*P*	Age-specific annual percentage change (%)	*P*	Sign of the second order term	*P*
30-34	5.42	<0.001	−	0.571	−0.75	<0.001	+	0.071
35-39	5.88	<0.001	+	0.271	−0.79	<0.001	−	0.783
40-44	6.23	<0.001	+	<0.001	0.29	<0.001	−	<0.001
45-49	6.41	<0.001	+	0.108	0.96	<0.001	−	<0.001
50-54	6.83	<0.001	+	<0.001	2.07	<0.001	−	<0.001
55-59	6.43	<0.001	+	0.091	1.93	<0.001	−	0.091
60-64	5.77	<0.001	+	0.003	1.69	<0.001	−	<0.001
65-69	5.07	<0.001	+	0.515	1.63	<0.001	−	<0.001
70-74	6.31	<0.001	−	0.540	1.91	<0.001	−	<0.001
75-79	7.28	<0.001	−	0.334	1.68	<0.001	−	<0.001
80-84	9.40	<0.001	+	0.127	1.35	<0.001	−	<0.001
30-84	6.68	<0.001	+	<0.001	1.25	<0.001	−	<0.001

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Table 2. Summary statistics comparing goodness-of-fit for different models

Model	Taiwanese				Caucasian Americans			
	df	Deviance	*P**	Adjusted R^2	*df*	Deviance	*P**	Adjusted R^2
Age	33	3,797.28			33	28,102.18		
Age-period	30	47.48	<0.001	0.986	30	4,899.42	0.001	0.808
Age-cohort	20	50.81	<0.001	0.978	20	4,881.68	<0.001	0.713
Age-period-cohort	18	10.26		0.995	18	1,100.31		0.928

*P value is based on the F test for comparison between any two-factor model and the full age-period-cohort model.

Western countries (20, 21). In Taiwan, there was also a drastic 30% to 40% reduction of fertility rate among women born in the 1970s compared with women born in the 1960s, whereas there were similar fertility rates between women born in the 1950s and 1940s (22). The reduced fertility rate in younger generations of Taiwanese women may partly contribute to the increased incidence of FIBC. In addition to the reduced fertility rate and earlier menarche, Taiwanese women born after the 1960s also had delayed child-bearing and decreased breast-feeding, indicating prolonged reproductive stimulation in their lifetimes. These factors have been linked with increased risk of female breast cancer in both epidemiologic studies in Taiwan and in Western countries (23-25).

The APC model has been widely used to analyze the trend of breast cancer incidence (11, 26-32). These studies all showed a strong birth cohort effect, suggesting the contribution of lifestyle and other possible environmental factors in the pathogenesis of breast cancer. Although some Western series found a moderation of breast cancer risk in birth cohorts born after World War II, the risk of breast cancer continues to increase in all Asian series. These findings suggest that as the birth cohort effect persists, breast cancer will become a more and more important public health problem in Asian countries.

Comparisons of the age distribution of FIBC in Taiwan, Hong Kong (8), and Japan (31), whose populations have experienced a similar trend of Westernization of lifestyle in recent decades, showed two distinctive patterns. In Taiwan and Japan, the peak incidence of breast cancer occurred mostly among individuals aged 45 to 49 years, and breast cancer was relatively uncommon in those aged 70 years or older. By contrast, in Hong Kong, the incidence of breast cancer continued to increase with age, a pattern similar to that seen in the U.S. and other Western countries. It has been suggested that exposure to risk factors in early life plays a critical role in subsequent risk of breast cancer (33, 34). Taiwan was colonized by Japan from 1895 to 1945 and the birth cohorts in Taiwan and Japan from that period of time may have shared similar lifestyles. Therefore, the similarity of age distribution of breast cancer in Taiwan and Japan may be more than a coincidence.

A significant period effect on the trend of FIBC incidence was also found in Taiwanese by the APC analysis. This may be partly due to improvement in completeness of the cancer registry data in the recent years. Other contributory factors include increasing self-awareness of breast cancer among women, successful public health education, and improvement in diagnostic tools. The population-based screening mammography program had not been initiated during this period in Taiwan, and its contribution to the increasing incidence of FIBC remains unclear.

We also showed a slight birth cohort effect and a negligible period effect on the trend of FIBC incidence in Caucasian Americans. Because of almost unchanged Western diet habits, changes in reproductive factors as a consequence of industrialization must make crucial contributions to the birth cohort effect. The change in relative risk by time period was only seen in the early 1980s, and was then negligible in subsequent years. It probably reflects the introduction of the population-based screening mammography program for women aged 40 years or older since 1980, which led to a significant increase of FIBC incidence, in particular, early diseases, in the early 1980s.

In conclusion, the incidence of FIBC in younger generations of Taiwanese is rapidly increasing and approaching that of Caucasian Americans. This trend seems to be a consequence of Westernization of lifestyles. The incidence and age distribution of FIBC might become increasingly similar to those of Caucasian Americans as Taiwanese women born after 1960s, who have been living an almost completely Westernized lifestyle, grow older.

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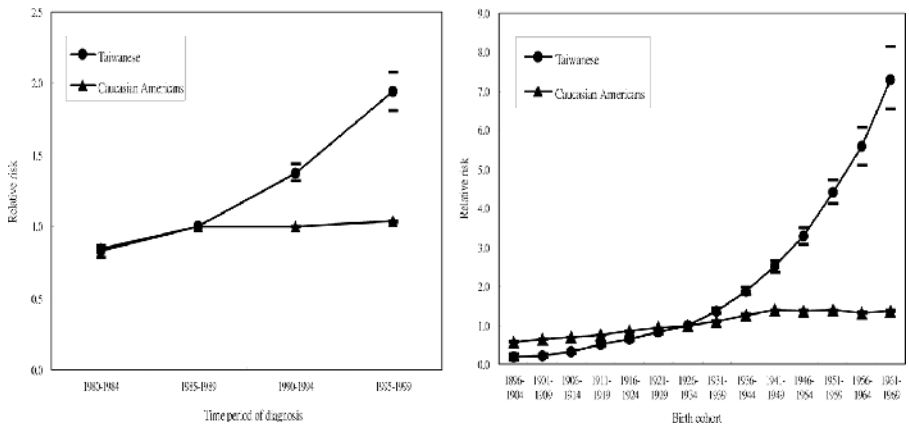

Figure 3. The relative risks and 95% confidence intervals by birth cohort and time period. Bars, 95% confidence intervals of the relative risk of Caucasian Americans was so small (<0.1) that it is not discernible in the figure.

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