行政院國家科學委員會專題研究計畫 期中進度報告

子計畫一 建立癌症研究的資料及統計中心

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Abstract

The objective of this study was to investigate the roles of spatio-temporal factors in the incidence and mortality of breast cancer among Taiwanese women from 1979 to 1998. Breast cancer incidence and mortality data were provided by Taiwan’s Department of Health (DOH). The spatial factors included urbanization, residential areas, population density and allocation of medical resources. The rate of increase of breast cancer incidence over the 20-year period was much higher than that of breast cancer mortality. Overall, the peak of breast cancer incidence was in the age range of 45 to 49 years. Breast cancer incidence in the 336 regions varied considerably and correlated strongly with mortality (r=0.37). Breast cancer incidence and mortality were strongly correlated with each of the four spatial factors. In conclusion, the significant differences in breast cancer incidence and mortality based on spatio-temporal factors indicate that environmental factors play an important role in the etiology of this disease. The results of this study may be used as a reference in strategies aimed at preventing breast cancer.

Keywords: Spatio-temporal factors, breast cancer incidence, mortality
摘要

此研究的目標在於調查空間時間因子在台灣女性乳癌的發生率和死亡率中所扮演的角色。研究期間為1979年至1998年。而乳癌的發生率和死亡率的資料來源為衛生署。空間因子包括都市化程度、地形、人口密度和醫療資源的分布。結果顯示女性年齡大於20歲其乳癌發生率的增加比死亡率來的高，而乳癌的發生率在45歲至50歲的期間達到巔峰，但是最近幾年發現，乳癌的發生率有逐漸年輕化的趨勢。此外，乳癌的發生率在336個鄉鎮市區中和死亡率有顯著的相關性，且研究發現乳癌的死亡率及發生率和四個空間因子有顯著的相關。整體而言，乳癌的死亡率和發生率在環境中的時空因子對乳癌的發生率和死亡率扮演著重要的角色，本研究的結果可提供有關機構作為預防乳癌政策上的參考及預防乳癌的目標。

關鍵字：時間空間因子、乳癌發生率、死亡率
Introduction

Breast cancer is a major cause of death among Taiwanese women. In 2000, breast cancer mortality rate among women was 10.61 per 100,000. There has been a steady rise in breast cancer incidence over the last twenty years which may reflect, in part, changes in lifestyle, such as diet. In 1990, Taiwan’s DOH implemented a nationwide breast cancer screening program in the community. Between 1999 and 2001, one million women aged over 35 years were given breast palpitation. The screening program included education about self-examining and the importance of early detection. Suspected positive cases were referred to local hospitals for diagnosis and treatment. Tabar (2003) investigated mortality in breast cancer patients and found that mammography service screening substantially reduced mortality rates. In Taiwan, such screening programs have not been comprehensively evaluated. Recent reports in Taiwan indicate that the age of onset of malignant breast cancer has become lower over the past few decades. Family history of breast cancer is a well-known risk factor in early onset of this disease. Claus (1990) conducted a population-based case-control study. A total of 4730 breast cancer patients were age- and residence-matched with 4688 controls. Family history of breast cancer, especially in a first-degree relative, was found to be a significant factor, after adjustment for confounders. Sattin (1985) found that risk of developing breast cancer was 2.3 times higher in patients with a
family history of breast cancer compared to those without family history of the
concluded that the lifetime excess incidence of breast cancer is 5.5% with one
affected first-degree relative and 13.3% for women with two. Although family history
most likely affects incidence of breast cancer through genetic predisposition, various
environmental factors may also play important roles. Currently, there are no available
data in Taiwan on relationships between the incidence and mortality of breast cancer.
Moreover, there are no data on the spatio-temporal factors that may affect incidence
and mortality of this disease in Taiwan. The findings of this study will be used to
establish baseline data on breast cancer incidence and mortality in order to develop
nationwide breast cancer prevention programs.

Materials and Methods

Data on the general population from 1979 to 1998 in Taiwan were provided by the
Ministry of the Interior, while data on breast cancer cases and breast cancer death
cases were provided by the Department of Health. Data from 1996 were used as the
standard population to calculate the standardized incidence and mortality of breast
cancer in each year. Standardized incidence and mortality in each district from 1992
to 1996 were categorized into five levels (>80%, 60-80%, 40-60%, 20-40%, <20%),
labeled as high risk, moderate high risk, moderate, moderate low risk and low risk. Urbanization data, residential areas, population density and medical resources (no. of medical staff) and population density were provided by the government office of statistics (Executive Yuan). The urbanization level was classified into seven categories according to population density, social index, and economic status. In the current study three main categories of urbanization were used: metropolitan (high), suburban (moderate) and rural areas (low). Residential areas were classified into three categories: plains, mountains and outlying islands. The proportions of the population and medical staff were calculated by dividing numbers in each district by numbers in the total population. These proportions were classified into high (over 33.3%), low (under 66.6%) and medium (between 33.3% and 66.6%). Population density in each district was calculated in the same way. Age-adjusted incidence and mortality were graded into five levels. Breast cancer incidence was graded from 0-11.95, 11.95-15.95, 15.95-20.75, 20.75-27.24, 27.24-67.46 per 100,000 population. Breast cancer mortality was graded from 0-3.93, 3.93-6.61, 6.61-8.41, 8.41-10.45, 10.45-26.25 per 100,000 population.

The statistical model used was proportional odds model

$$\log(\text{ODD}_{j(x)}) = \alpha_j + \beta_1 x_1 + \beta_2 x_2 + \Lambda + \beta_k x_k,$$

where $x$ meant spatial factors, $j$ represented the mortality or incidence level
Since the assumption of proportional odds hold (which was shown by the goodness-of-fit test for model fit), for any fixed $j$, the estimated odds that a spatial situation (denoted by $A$) is in the high risk direction rather than the low risk direction equal $\exp(\beta)$ times the estimated odds for the other spatial situation (denoted by $B$).

For example, for urbanization, let $x=A$ meant in the moderate urbanization area, $x=B$ meant in the low urbanization area, the odds ratio (OR) was calculated from these results as follows:

$$
\text{Odds Ratio} = \frac{\frac{p_5(x=A)}{1-p_5(x=A)}}{\frac{p_5(x=B)}{1-p_5(x=B)}} = \frac{\frac{p_4(x=A)}{1-p_4(x=A)}}{\frac{p_4(x=B)}{1-p_4(x=B)}} = \frac{\frac{p_3(x=A)}{1-p_3(x=A)}}{\frac{p_3(x=B)}{1-p_3(x=B)}} = \frac{\frac{p_2(x=A)}{1-p_2(x=A)}}{\frac{p_2(x=B)}{1-p_2(x=B)}}.
$$

When OR was over 1, this meant that the population in the moderate urbanization area had a higher risk of developing breast cancer than the population in areas with low level urbanization. The same calculation method was used for the other spatial factors. Age standardized incidence and mortality were plotted for each year (1979 to 1998), for each age group, and for each birth cohort. Age standardized incidence and mortality of breast cancer in the 336 districts were calculated and classified into five categories and plotted on the map of Taiwan. The Pearson’s correlation coefficient between incidence and mortality was calculated.
Results

Age standardized incidence and mortality of breast cancer in the 336 districts in Taiwan are shown in Figure 1. Breast cancer incidence and mortality were graded into five levels with the darkest areas indicating highest incidence and mortality. The darkest areas tend to coincide with the metropolitan areas, such as in the north. Pearson’s correlation coefficient between incidence and mortality of breast cancer was 0.37. Incidence was lowest in the east of Taiwan, although some areas with low breast cancer incidence had high mortality.

Figure 2 shows the trends in age-specific breast cancer incidence and mortality rates from 1979 to 1998. Incidence of breast cancer increases with time, with a sharp increase at 1990. However, the mortality rate increases only slightly (range from 5/100,000 population to 10/100,000 population). The peak in mortality rate occurred in 1997 and decreased gradually afterwards.

Figure 3 shows the trends in age-specific incidence and mortality rates of breast cancer by birth cohort (1902-1911, 1907-1916, ..., 1942-1951). Incidence of breast cancer occurred at an earlier age in the younger generations. Also, the rate of increase in incidence of breast cancer was higher in the younger generations.

There was a similar trend to that in Fig.3 with an increase of breast cancer mortality with age. The increase in incidence was highest in the most recent five-year time period (1992-1996), with a peak at 45-49 years for each five-year age interval. In principle, mortality rates increased in each of the three five-year time periods. Mortality rate was highest at ages over 80 years. Except for ages over 80 years, the mortality in the most recent five-year time period was consistently higher than in the other time periods. For all ages below 65, incidence of breast cancer was higher than breast cancer mortality.

Table 1 shows the correlations of the five levels of breast cancer incidence and mortality with the spatial factors. Overall, there were significant associations of both incidence and mortality of breast cancer with each of the spatial factors. There was a significant positive correlation of high urbanization with breast cancer incidence and mortality. There was an even spread of levels of breast cancer incidence and mortality in the plain areas, but for the mountainous areas and outlying islands, there were negative correlations with breast cancer incidence and mortality. Population density correlated negatively with breast cancer incidence and mortality. Low population density correlated significantly with high incidence of breast cancer, but breast cancer mortality was similar in each level of mortality at low population density. There was a positive correlation of medical resources with breast cancer incidence and mortality.
The odds ratios of breast cancer incidence and mortality within levels of each spatial factor can be seen in Table 2. There were dose-dependently significant correlations of urbanization with breast cancer incidence and mortality. There was a significant difference between plains and mountains in breast cancer incidence and mortality, but there were no significant associations among other topographical areas. Significant negative correlations between each of the levels of population density were found in breast cancer incidence, but for breast cancer mortality only high and low population density correlated significantly. High level of medical resources was higher than medium and low levels of medical resources in both breast cancer incidence and mortality. Incidence and mortality of breast cancer were similar between medium and low level of medical resources.

**Discussion**

Previous studies of breast cancer in Taiwan have shown that breast cancer mortality is highest in urban areas, while it is highly variable around the island as a whole, which may be due to the small number of breast cancer cases. Long-term monitoring of breast cancer mortality is required to identify trends in different parts of the country. In addition, cancer mapping, such as the “Geographic Information System” (GIS) can provide a dynamic exhibition of patterns and trends which yields information about the clustering and diffusion process in breast cancer mortality and incidence, as well
their intercorrelations. The current study found that breast cancer mortality and incidence were highly correlated and has increased gradually over the past twenty years. This may be attributed to the introduction of the national cancer screening program in 1995 in Taiwan. Furthermore, dietary and lifestyle changes may have contributed to the increase in breast cancer mortality and incidence. Another important trend is the considerably earlier onset of breast cancer incidence over the past twenty years. As such, the Department of Health may lower the age of breast cancer screening. Ongoing health awareness programs have also helped to catch breast cancer in many women in Taiwan. Levi (1994) reported that overall incidence of various cancers increased from 10% to 30% but the cancer mortality remained approximately the same. This may be due to improved diagnosis and therapeutic advancements. Menegoz (1997) investigated the cancer incidence and mortality in France in 1975-95 and found that mortality remained relatively even while incidence increased.

Cancer mapping studies have shown that the south-west of Taiwan has a clustering effect for certain cancers, such as cancer of the bladder, skin, liver and lung which have been attributed to arsenic in the groundwater. However, breast cancer incidence in this part of the country was not significantly from that in other areas. Factors other than lifestyle and diet that affect breast cancer incidence include
pesticides, such as DDT which was used 50 years ago to eradicate malaria in Taiwan, and air pollutants from incinerators, such as dioxin. The Taiwan EPA has recently reduced the maximum permissible limit for dioxin. Breast cancer incidence is generally much higher in highly urbanized areas. This finding is consistent with those of many other studies in other countries, such as Japan and Spain. Previous studies have identified other factors associated with increased incidence of breast cancer, such as decreasing age of menarche, increasing age at first marriage, age at first birth, decreasing fertility rate and increasing adult height. Minami (1996) reported significant period effects on breast cancer incidence, although the cohort effect was marginal. The relative risks by birth cohort suggested a declining trend in younger birth cohorts. Mackillop (2000) evaluated associations between community incomes and cancer incidence in North America and found that breast cancer incidence was highest among highest socioeconomic status, although the underlying mechanisms remain unclear. Over the years the cancer registry has developed comprehensive data on breast cancer. In addition, breast cancer diagnostic techniques have improved considerably, as proven by follow-up biopsy in 80% of diagnoses. This database can be used to correlate with environmental and ecological factors as well as personal risk factors, such as predisposition, alcohol consumption and smoking habit. Analyses of the significant associations are vital in the development of national cancer prevention
programs. The database can also be used to evaluate the effectiveness of such programs.

ACKNOWLEDGEMENTS

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REFERENCES


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Table 1. Correlations of the five levels of breast cancer incidence and mortality with the spatial factors (1992 to 1996)

<table>
<thead>
<tr>
<th>Spatial factors</th>
<th>Rate of Incidence rate (%)</th>
<th></th>
<th>Rate of Mortality (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
<td>Mod</td>
<td>Mod</td>
<td>High</td>
</tr>
<tr>
<td>Urbanization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>168</td>
<td>35.7</td>
<td>24.4</td>
<td>19.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>7.7</td>
<td>20.3</td>
<td>23.8</td>
<td>27.3</td>
</tr>
<tr>
<td>High</td>
<td>48</td>
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<td>Region</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Outlying islands</td>
<td>9</td>
<td>22.2</td>
<td>44.4</td>
<td>11.1</td>
</tr>
<tr>
<td>Mountainous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>areas</td>
<td>65.5</td>
<td>13.8</td>
<td>10.3</td>
<td>6.9</td>
</tr>
<tr>
<td>Plain areas</td>
<td>321</td>
<td>15.6</td>
<td>19.9</td>
<td>21.2</td>
</tr>
<tr>
<td>Pop. Density</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>119</td>
<td>13.4</td>
<td>10.9</td>
<td>16.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>120</td>
<td>14.2</td>
<td>23.3</td>
<td>23.3</td>
</tr>
<tr>
<td>High</td>
<td>120</td>
<td>31.7</td>
<td>25.8</td>
<td>20.0</td>
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<td>Dist. of Medical</td>
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</tr>
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<td>Resources</td>
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<td></td>
</tr>
<tr>
<td>Low</td>
<td>119</td>
<td>23.5</td>
<td>26.9</td>
<td>22.7</td>
</tr>
<tr>
<td>Moderate</td>
<td>120</td>
<td>25.8</td>
<td>20.8</td>
<td>18.3</td>
</tr>
<tr>
<td>High</td>
<td>120</td>
<td>10.0</td>
<td>12.5</td>
<td>19.2</td>
</tr>
</tbody>
</table>

#P : P value is according to chi-square tendency test

r* : r denotes Pearson’s correlation coefficient
Table 2. Odds ratios of breast cancer incidence and mortality within levels of each spatial factor (1992 to 1996)

<table>
<thead>
<tr>
<th>Spatial factor</th>
<th>Incidence rate</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratios (95% CI)</td>
<td>P</td>
</tr>
<tr>
<td><strong>Urbanization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>2.9 (1.9-4.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>High</td>
<td>22.4 (11.2-45.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outlying islands</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mountainous areas</td>
<td>1.3 (0.3-5.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>Plain areas</td>
<td>3.4 (1.0-11.8)</td>
<td>0.054</td>
</tr>
<tr>
<td><strong>Pop. Density</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>0.4 (0.3-0.7)</td>
<td>0.010</td>
</tr>
<tr>
<td>High</td>
<td>0.2 (0.1-0.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Distribution of Medical Resources</strong></td>
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<td></td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>1.4 (0.9-2.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>High</td>
<td>3.8 (2.4-6.0)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

P: P value is according to chi-square test
Figure 1. Age standardized incidence and mortality of breast cancer in the 336 districts in Taiwan.

*\(r\): Pearson’s correlation coefficient between incidence and mortality
Figure 2. Trends in age-specific breast cancer incidence and mortality rates from 1980 to 1998.
Figure 3. Trends in age-specific incidence and mortality rates of breast cancer by year of birth
Figure 4. Trends in age-specific incidence and mortality rates of breast cancer in three five-year time periods.
五月十一號

台灣地區縣市區癌症死亡率及發生率逐年趨勢
與地區網頁查詢系統的建立

重要癌症發生與死亡的空間分類查詢系統

重要癌症發生和死亡與環境因子關聯的空間分類查詢系統的建立。

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