A discussion of association between the risks on breast and liver cancer for women based on data given by age and period

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Abstract

In the previous experimental and epidemiological studies it has been accepted that, in the presence of estrogen, higher doses of dietary soy isoflavones may alter estrogen receptors signaling and induce selective antagonistic effects in the breast, that is, the risk of breast cancer death for women can be decreased by their isoflavone intake. On the other hand several researchers are issuing an alert that women who eat a lot of soybean products are three to four times more likely to develop liver cancer than those who eat only a small amount, that is, high isoflavone intake increases the risk of liver cancer for women. So our aim in this study is to exam such an association between the risks on breast and liver cancer for women from the analysis of nationwide census data.

The result of fitting a model, which is an alternative to age-period-cohort model, to data for death of breast and liver cancer shows that there exist environmental factors which decrease the risk of breast cancer and increase the risk of liver cancer for women. This result may suggest the existence of effect of women’s isoflavone intake on death of those two cancers on a nationwide scale.

Key words: Age-period-cohort model, effect of isoflavone intake, environmental factor

1. Introduction

Breast cancer is one of serious illness for women, is the #1 cause of death for women aged 30-50. Therefore, various preventive measures have been noted. In the previous experimental and epidemiological studies it has been accepted that, in the presence of estrogen, higher doses of dietary soy isoflavones may alter estrogen receptors signaling and induce selective antagonistic effects in the breast, that is, the risk of breast cancer death for women can be decreased by their isoflavone intake (Charles E.Wood et al. 2006).

On the other hand several researchers are issuing an alert that women who eat a lot of soybean products are three to four times more likely to develop liver cancer than those who eat only a small amount, that is, high isoflavone intake increases the risk of liver cancer for women (http://www.hepcaustralia.com.au/symptoms-news/high-soybean-consumption-increases-risk-of-liver-cancer-in-women-survey). This fact is considered because estrogen heightens the risk of breast cancer while it protects against liver cancer. Thus it is believed that excessive consumption of isoflavones may block this property. It is noteworthy that this property is said to be particularly in postmenopausal women.

For instance, the data for death rates of breast and liver cancer per 100 thousands Japanese women aged 55-59, it showed a strong negative correlation -0.89 as indicated in Figure 1. But it cannot be denied the possibility of spurious correlation. So, our aim In this study is to examine whether there exist environmental factors which decrease the breast cancer risk and increase the liver cancer risk for postmenopausal females aged 55 and over based on more rigorous analysis of more specific data, that is, (age, period)-tabulated data, which is indicated in Table 1 for liver cancer.

In the next Section 2 our procedure and model to examine whether there exist environmental factors which decrease the breast cancer risk and increase the liver cancer risk are introduced. The following Section 3 the results of applying our
procedure to the data are shown and the agendas on our procedure are discussed in the final Section 5.

**Death rates of breast and liver cancer per 100 thousands Japanese women aged 55-59**

![Figure 1. Death rates of breast and liver cancer](image)

**Table 1. Deaths of liver cancer in 100 thousand Japanese males aged 55 and over**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>55~59</td>
<td>1970-74</td>
<td>14.5</td>
<td>13.7</td>
<td>12.7</td>
<td>13.7</td>
<td>12.5</td>
<td>10.5</td>
<td>8.2</td>
<td>6.3</td>
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<tr>
<td></td>
<td>1975-79</td>
<td>22.8</td>
<td>21.1</td>
<td>21.8</td>
<td>23.0</td>
<td>25.0</td>
<td>26.4</td>
<td>18.4</td>
<td>12.7</td>
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<tr>
<td></td>
<td>1980-84</td>
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<td>32.3</td>
<td>35.4</td>
<td>38.4</td>
<td>47.2</td>
<td>40.4</td>
<td>27.0</td>
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<tr>
<td></td>
<td>1985-89</td>
<td>50.5</td>
<td>46.9</td>
<td>46.6</td>
<td>48.6</td>
<td>51.9</td>
<td>62.0</td>
<td>64.4</td>
<td>54.5</td>
</tr>
<tr>
<td></td>
<td>1990-94</td>
<td>66.4</td>
<td>62.1</td>
<td>63.9</td>
<td>62.0</td>
<td>65.6</td>
<td>75.6</td>
<td>78.9</td>
<td>78.1</td>
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</table>

### 2. Procedure and model

As describe in the previous section our aim in this study is to examine whether there exists an upper limit of human longevity based on the analysis of data for oldest old survivors and deaths given by age and period. For that purpose it is needed to exclude the period and age effect from data given by age and period. So the following procedure is conceived:

1. estimating the environmental risks of breast cancer and liver cancer for female based on (age, period)-tabulated data,
2. testing for the significance of the correlation coefficient between environmental risks for breast cancer and liver cancer.

The above is one idea of procedure for examining our supposition, however, it is well known that hepatitis C virus infection is the main causes of liver cancer. So it is needed to eliminate the effect of infection to hepatitis C virus from environment effects. For this purpose we focus on the following findings: In women, genistein and daidzein were dose-dependently associated with an increased risk of hepatocellular carcinoma (HCC, liver cancer), while no association between isoflavones and HCC was observed in men (Kurahashi et al. 2009). Referring that fact we suppose that the difference of environmental effect on liver cancer between men and women is effect of isoflavone on breast cancer for women, the following modified procedure comes up:

1. estimating the environmental risks of breast cancer for female and liver cancer for both sexes,
2. calculating difference of environmental risks between men and women for liver cancer,
(3) testing for the significance of the correlation coefficient between environmental effects on breast cancer and the difference of environmental effect on liver cancer between men and women.

As for the environmental risks of breast or liver cancer it is estimated by applying the age period environment model introduced in the followings.

As mentioned in Table 1 our data to be analyzed in this study, it observed by age and period (age-by-period data). So let $D_{ij}$ ($i = 1, \cdots, I; j = 1, \cdots, J$) be a random variable that indicates the number of deaths who are in the $i$th age interval $[A_{i-1}, A_i)$ in the $j$th period $[P_{j-1}, P_j)$ whether $P_j - P_{j-1} = A_i - A_{i-1} = 5$. the number of deaths $D_{ij}$ is illustrated on the Lexis diagram indicated in the Figure 1 where vertical axis indicates age and horizontal axis indicates time and $D_{ij}$ is corresponding to the squared area.

![Figure 2 Lexis diagram](image)

Then our model applied to the age-by-period data for estimating environmental risk on breast and liver cancer is expressed as follows:

$$\log \eta_{ij} \equiv \log \frac{E[D_{ij}]}{N_{ij}} = \mu + \alpha_i + \beta_j + \sum_{k=j-1+1}^{j-1} \xi_k,$$

where $N_{ij}$ is the person-years corresponding to $D_{ij}$, $\alpha_i$ is age effect, $\beta_j$ is period effect and $\xi_k$ is environment effect on $\eta_{ij}$. Those three effects are illustrated in Figure 3.

![Figure 3 Illustration of $\alpha_i$, $\beta_j$ and $\xi_k$ on the Lexis diagram](image)

Further, differences in period effects and environmental effects is given in Figure 4.
As seen from Figure 4 the environmental effect $\beta_j$ is considered as a remaining effect of exposure to the environmental risks in the period $[P_{j-1}, P_j]$ while the period effect $\tilde{\beta}_j$ is an immediate effect of them.

3. Results

3.1. Result of estimating the environmental risks of breast

![Figure 5. Environmental effect on breast cancer (Female)](image)

![Figure 6. Environment effect on liver cancer (Female)](image)
3.2. Result of calculating difference of environmental risks

![Figure 7. Environment effect on liver cancer (Male)](image)

Figure 7. Environment effect on liver cancer (Male)

3.3. Result of calculating difference of environmental risks

As shown in Table 2 environmental effects on breast cancer in women and the difference of environmental effect on liver cancer between men and women significantly have a negative correlation with P-value of -0.62.

![Figure 8. Difference of environmental effect on liver cancer between sexes](image)

Figure 8. Difference of environmental effect on liver cancer between sexes

![Figure 9. environmental effects on breast cancer and the difference of environmental effect on liver cancer between men and women](image)

Figure 9. environmental effects on breast cancer and the difference of environmental effect on liver cancer between men and women
Table 2. Correlation coefficient between environmental effects on breast cancer and the difference of environmental effect on liver cancer between men and women

<table>
<thead>
<tr>
<th>Correlation Coefficient</th>
<th>t Stat</th>
<th>P-value</th>
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<tbody>
<tr>
<td>-0.62</td>
<td>-2.37</td>
<td>0.04</td>
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4. Conclusion

It has been shown that there exist environmental factors which decrease the breast cancer risk and increase the liver cancer risk for postmenopausal females aged 55 and over.

Reference

Charles E. Wood1, Thomas C. Register1, Adrian A. Franke2, Mary S. Anthony1, and J. Mark Cline1 Cancer Res 2006; 66:1241-1249.