GASTRIC CANCER RISK FACTORS: A CASE-CONTROL STUDY BASED ON MEDICAL RECORDS

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Four hundred and sixty gastric cancer patients who had undergone operation at the National Cancer Center Hospital and an equal number of age-matched controls were analyzed in order to estimate the influence of gastric cancer family inheritance and cigarette smoking habit. Relative risks for cigarette smoking habit, for gastric cancer family inheritance and for both were 2.88, 1.67 and 4.12, respectively. Earlier age of onset of gastric cancer was observed in the gastric cancer cases with both risk factors as compared with the other patients.

Key words: Gastric cancer family inheritance — Cigarette smoking habit — Relative risk — Case-control study

Since most case-control studies on the high risk factors of gastric cancer so far performed have been largely oriented to the elucidation of individual risk factors,1,2 the interaction between such factors is not yet well understood. Hirayama reported an earlier age of onset of gastric cancer among gastric cancer-prone families.3 He also reported the attributable risk of cigarette smoking habit as 26.4%.4 Lynch reported the "cancer family syndrome" and claimed that the incidence of gastric cancers in the cancer family was 3 times higher than that in the general population; he also reported an earlier age of onset of gastric cancer in the cancer family.5 Yanai et al. investigated the interaction between multiple risk factors of gastric cancer by multiple variance analysis,6 and reported a higher incidence of gastric cancer in the 30's age group in the cancer family, as well as a higher risk in all age groups of heavy smokers. Our experiments on animal syncarcinogenesis prompted us to analyze the risk factors with particular attention to the interaction between them for human gastric carcinogenesis.7,8

MATERIALS AND METHODS

Four hundred and sixty gastric cancer patients who had undergone operation at the National Cancer Center Hospital during 1979-1982 and the same number of controls examined in the Adult Disease Clinics*11 were matched for sex, age (under 59 years and over 60 years) and family history of cancer (Table I).9 Further, we divided the so-called cancer families into gastric cancer families and other cancer families (Tables II and III). Gastric cancer patients with 1st to 3rd degree relationships to gastric cancer probands were included in such families. Items examined in these clinics are similar to those routinely checked at the National Cancer Center Hospital. Although risk factors such as obesity, alcohol drinking, previous medical histories, etc. are known, in the present study attention was focussed on gastric cancer family inheritance and cigarette smoking habit only. Cigarette smoking habit and family history of cancer were obtained through at least three pro-
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Table I. Gastric Cancer Cases and Age-matched Controls with or without Family History

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Gastric cancer $,^{(a)}$</th>
<th>Control $,^{(a)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer family history $,^{(-)}$</td>
<td>Cancer family history $,^{(+)}$</td>
</tr>
<tr>
<td>Total</td>
<td>230</td>
<td>230</td>
</tr>
<tr>
<td>$\leq 59$</td>
<td>115</td>
<td>115</td>
</tr>
<tr>
<td>$\geq 60$</td>
<td>115</td>
<td>115</td>
</tr>
</tbody>
</table>

(a) National Cancer Center Hospital.

Table II. Gastric Cancer Cases and Controls with or without Family History (Male)

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Gastric cancer</th>
<th>Control</th>
<th>Relative risk of gastric cancer for those with gastric cancer family history $,^{(a)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer family history $,^{(-)}$</td>
<td>Gastrointestinal cancer family history $,^{(+)}$</td>
<td>Other cancer family history $,^{(+)}$</td>
</tr>
<tr>
<td>Total</td>
<td>230</td>
<td>139</td>
<td>91</td>
</tr>
<tr>
<td>$\leq 59$</td>
<td>115</td>
<td>73</td>
<td>42</td>
</tr>
<tr>
<td>$\geq 60$</td>
<td>115</td>
<td>66</td>
<td>49</td>
</tr>
</tbody>
</table>

(a) Relative risk was calculated by taking the risk of gastric cancer cases without gastric cancer family history as the unit.

(b) Relative risk $= \frac{73}{42} \times \frac{49}{64} \times \frac{115}{115} = 2.27$.

(c) Relative risk $= \frac{66}{49} \times \frac{57}{58} \times \frac{115}{115} = 1.37$.

Table III. Gastric Cancer Cases and Controls with or without Gastric Cancer Family History (Male)

<table>
<thead>
<tr>
<th>No. of cigarettes per day</th>
<th>Age</th>
<th>$\leq 59$</th>
<th>$\geq 60$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer family history $,^{(-)}$</td>
<td>Gastrointestinal cancer family history $,^{(+)}$</td>
<td>Other cancer family history $,^{(+)}$</td>
</tr>
<tr>
<td>No cigarette</td>
<td>21/41</td>
<td>21/28</td>
<td>11/34</td>
</tr>
<tr>
<td>$\leq 19$</td>
<td>22/16</td>
<td>11/5</td>
<td>9/13</td>
</tr>
<tr>
<td>$\geq 20$</td>
<td>72/58</td>
<td>41/18</td>
<td>22/17</td>
</tr>
</tbody>
</table>

Cancer cases, 460; controls, 460.

At the Adult Disease Clinics, at least three procedures were also undertaken to obtain details of cigarette smoking habit and family history of cancer. Firstly the patients had been requested to fill out questionnaires on many items including cigarette smoking habit and family history of cancer. Secondly the attending physicians had checked the questionnaires and examined the patients. Thirdly, after the completion of the physical examination, a final interview was done with each patient. The attending physicians confirmed the information...
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on cigarette smoking habit and family history of cancer.

The relative risk was calculated according to the Schlesselman method\(^{10}\) taking the risk of gastric cancer in cases without gastric cancer family history or smoking habit as the unit.

**RESULTS**

**Analysis of the Whole Group (Irrespective of Age)** Relative risks of gastric cancer in subjects without cancer family history and smoking habit, in those with cancer family history alone, in those with smoking habit alone and in those both with cancer family history and smoking habit were 1.0, 1.65, 3.08 and 4.24, respectively. The relative risk of cancer family history alone was not statistically significant (\(\chi^2=3.34\)) (Fig. 1). However, if gastric cancer cases with family history of other cancers were considered as having no cancer family history (i.e., no gastric cancer family history), the relative risks of gastric cancer in subjects without gastric cancer family history and smoking habit, those with gastric cancer family history alone, those with smoking habit alone, and those both with gastric cancer family history and smoking habit became 1.0, 1.67, 2.88 and 4.3, respectively. The relative risk of gastric cancer in cases with gastric cancer family history alone was statistically significant (\(\chi^2=4.37\)) as compared with cases without gastric cancer family history and smoking habit.

**Analysis by Age Groups** Relative risks of gastric cancer in subjects with or without smoking habit at age under 59 years and over 60 years are shown in Fig. 2. Relative risks of gastric cancer in subjects with gastric cancer family history alone at age under 59 years and over 60 years were 1.76 and 1.62, respectively. Relative risks in those without gastric cancer family history and with smoking habit under 59 years of age and over 60 years of age were 2.83 and 3.08, respectively. Relative risks in those with both gastric cancer family history and smoking habit at under 59 years and over 60 years of age were 5.30 and 3.49, respectively. The relative risk of gastric cancer in subjects with gastric cancer family history and smoking habit under 59 years of age was statistically significant compared with cases with gastric cancer family history alone or smoking habit alone at age under 59 years. These findings might reflect the effect of syncarcinogenesis induced by both risk factors.

**DISCUSSION**

Relative risk of gastric cancer in subjects with both gastric cancer family history and cigarette smoking habit was markedly ele-
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compared with the relative risk of gastric cancer in subjects with gastric cancer family history alone, cigarette smoking habit alone or without both. Elevated risk of gastric cancer was also found in male gastric cancer cases under 59 years old with gastric cancer family history and cigarette smoking habit as compared with similar groups of over 60 years of age.

Environmental factors are as influential as genetic factors in gastric carcinogenesis, as shown in a study on immigrants in Hawaii. Among the environmental factors, cigarette smoking habit seems to play one of the most important roles in gastric carcinogenesis. We could see an augmented relative risk based on the sum of the relative risks of gastric cancer risk factors, cigarette smoking habit and genetic factors.

The three degrees of relatives of gastric cancer probands and the controls were studied in this report. In the future, the possible role of gastric cancer inheritance within blood relatives should be more systematically investigated. Cigarette smokers should be classified by the number of cigarettes smoked. If controls were obtained from the same hospital, the comparability of cases and controls would be improved. Further studies are required, taking these points into consideration.

ACKNOWLEDGMENTS

We wish to express our appreciation to Dr. K. Suemasu, Assistant Director of the National Cancer Center Hospital, and M. Shiraishi, Director of the Vital Statistics Division of the Ministry of Health and Welfare, for their kind advice. This investigation was supported by a grant from the Adult Disease Clinic Memorial Foundation of Japan.

(Received April 5, 1985/Accepted June 26, 1985)

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