



RAPID COMMUNICATION

## Risk factor analysis for metaplastic gastritis in Koreans

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### Abstract

**AIM:** To conduct a retrospective study to determine the risk factors for development of metaplastic gastritis in Korean population.

**METHODS:** The database of 113 449 subjects who underwent a gastroscopy for the purpose of a regular check-up at center for health promotion, Samsung medical center during 5 years was collected and retrospectively analyzed. Among them, 5847 subjects who had endoscopically diagnosed as a metaplastic gastritis or 10 076 normal as well as answered to questionnaire were included for present study. The subjects were divided into 2 groups; Group I, normal and Group II, metaplastic gastritis. Age, gender, *Helicobacter pylori* (*H. pylori*) seropositivity, body mass index (BMI), family history of cancer, smoking, alcohol consumption, total daily calories, folate and salt intake and dietary habit (out-eating, overeating, irregular eating) were retrieved from questionnaire or electronic medical record and compared between group I and group II.

**RESULTS:** The prevalence of group II was 11% (13 578/113 449) increasing its prevalence with age ( $P=0.000$ ). But, there was no significant association between 2 groups in BMI, family history of cancer, alcohol consumption, total daily calories, folate and salt intake and dietary habit (out-eating, overeating, irregular eating). Old age ( $P=0.000$ ), male gender ( $P=0.000$ ), *H. pylori* seropositivity ( $P=0.010$ ) and current smoker ( $P=0.000$ ) were significantly more common in group II at multiple logistic regression model.

**CONCLUSION:** Our data suggested that old age, male gender, *H. pylori* seropositivity and smoking were risk factors for metaplastic gastritis, precancerous lesion of gastric cancer.

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**Key words:** Intestinal metaplasia; Risk factors

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### INTRODUCTION

Gastric cancer was recognized as the first leading cause of cancer death in Korea<sup>[1]</sup> and attention turned to epidemiologic associations between risk factors and gastric cancer. In the early 1970s, Correa formulated a multi-step model of gastric cancer, which postulated a temporal sequence of pathologic changes that led from chronic gastritis to atrophic gastritis, intestinal metaplasia and dysplasia and the eventual development of gastric cancer<sup>[2]</sup>. Chronic gastric inflammation seems to be the critical common cause of gastric cancer<sup>[3]</sup>.

The purpose of this paper was to determine the risk factors for development of metaplastic gastritis, precursor of gastric cancer in Korean population

### MATERIALS AND METHODS

#### Data collection

The database of 113 449 subjects who underwent a gastroscopy for the purpose of a regular check-up at center for health promotion, Samsung medical center from January 2001 through June 2004 was collected and retrospectively analyzed. Among them, 13 578 subjects were endoscopically diagnosed as a metaplastic gastritis and 10 521 subjects was endoscopically diagnosed as a normal. But, only 5847 subjects who had endoscopically diagnosed as a metaplastic gastritis were answered to questionnaire whereas 10 076 subjects who had endoscopically diagnosed as a normal were answered to questionnaire. Both 5847 metaplastic gastritis and 10 076 normal were included for present study. Subjects with peptic ulcer or erosion of stomach were excluded in this study population. The subjects were divided into 2 groups; Group I, normal and Group II, metaplastic gastritis. Demographic data [age, gender, body mass index (BMI), family history of cancer] and life style data [smoking, alcohol consumption, total daily calorie intake, folate intake, salt intake, dietary habit (out-eating, overeating, irregular eating)] were retrieved from question-

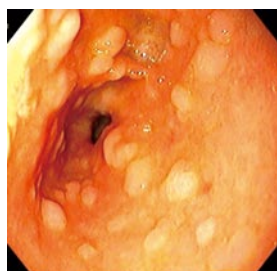


Figure 1 Endoscopic finding showed that atrophic mucosa with surface nodularity was generally diagnosed as a metaplastic gastritis.

naire or electronic medical records and compared between group I and group II. Those who have family history of any cancer were those who had a reply to yes in the question ("Do you have a blood relation who has a experience of diagnosis as cancer by a doctor?"). Data including smoking, alcohol consumption (frequency and amount of alcohol), dietary habit (out-eating, overeating, irregular eating) were collected from self administered questionnaire. Patients were asked whether they were active, past or never smoker. The subjects were divided into two groups (current smoking group and non-smoking group) by current smoking status. Nonsmoking group is composed of past or non-smoking. The subjects were divided into two groups by frequency and amounts of liquors (namely, *so-ju*) consumption in questionnaire. Over or equal 3-4 frequencies a week and  $\geq 80$  g once alcohol consumption is defined as the group of heavy alcohol consumption. Below 3-4 frequencies a week or  $<80$  g once alcohol consumption is classified as the other group. Total amount of calorie, folate intake and fat intake were obtained in diet surveys. *Helicobacter pylori* (*H. pylori*) seropositivity was retrieved from electronic medical record. *H. pylori* infection was determined by measuring serum *H. pylori* IgG antibodies. Specific anti-*H. pylori* antibodies were measured with an enzyme-linked immunosorbent assay (ELISA) kit using an antigen (RADIM SpA, Pomezia, Italy). The sensitivity and specificity of this assay was reported to be 79% and 83%, respectively<sup>[4]</sup>.

### Criteria for metaplastic gastritis

Atrophic mucosa with surface nodularity on the endoscopic finding was diagnosed as metaplastic gastritis (Figure 1). 3354 individuals who showed endoscopically metaplastic gastritis had also a presence of metaplasia histologically on the updated Sydney system.

### Statistical analysis

Logistic regression analysis was conducted by fixing the each group as a dependent variable and risk factors as independent variables. Continuous variables such as age, BMI, total daily calorie intake, folate intake and salt intake were analyzed by *t*-test. Gender, smoking, alcohol consumption, family history of cancer, dietary habit (out-eating, overeating, irregular eating) and *H. pylori* seropositivity were analyzed by  $\chi^2$  test. The relative risk to develop metaplastic gastritis was calculated with odds ratio with 95% confidence interval. Risk factors were examined by multiple logistic regression analysis. Statistical significance was assumed at  $P < 0.05$ . Statistical analyses were performed with SAS version 8.1 (SAS Institute Inc, Cary, NC, USA).

Table 1 Comparison of characteristics of normal and metaplastic gastritis (simple logistic regression model)

	Normal (%)	Metaplastic gastritis (%)	P value
Age	42.46 $\pm$ 10.15	53.20 $\pm$ 9.00	0.000
Sex			0.000
Men	3804 (36)	3983 (68)	
Women	6272 (64)	1864 (32)	
BMI <sup>1</sup>	24.52 $\pm$ 2.36	23.97 $\pm$ 2.86	0.208
Family history of cancer	160 (1)	125 (2)	0.065
Smoking			0.000
None or past	2933 (84)	3308 (74)	
Current	550 (16)	1130 (26)	
Alcohol			0.059
Heavy alcoholics <sup>2</sup>	553 (15)	747 (16)	
Out-eating	2477 (23)	1535 (26)	0.110
Over eating	1743 (16)	912 (15)	0.598
Irregular eating	1824 (17)	1152 (19)	0.228
Total calories	2102.94 $\pm$ 470.17	2226.46 $\pm$ 486.22	0.515
Folate	246.34 $\pm$ 91.24	289.51 $\pm$ 108.55	0.211
Salts	22.48 $\pm$ 7.27	23.02 $\pm$ 4.97	0.319
<i>H. pylori</i> seropositivity <sup>3</sup>	4165 (39)	3566 (60)	0.007

<sup>1</sup>BMI, body mass index.

<sup>2</sup>Over or equal 3-4 frequencies a week and  $\geq 80$  g once alcohol consumption is defined as the group of heavy alcoholics.

<sup>3</sup>*Helicobacter pylori* is abbreviated as *H. pylori*.

## RESULTS

### Characteristics of study subjects (Table 1)

The prevalence of group II was 11% (13 578/113 449) increasing its prevalence with age ( $P = 0.000$ ). But, there was no significant association between 2 groups in BMI, alcohol consumption and family history of cancer. Male gender was a risk factor for metaplastic gastritis and current smokers were more likely to have metaplastic gastritis than none or past smokers. Neither dietary composition (folate, salts, calories) nor dietary habits (out-eating, overeating, irregular eating) was associated with metaplastic gastritis. *H. pylori* seropositivity was more common in the group II.

### Multiple logistic regression analysis (Table 2)

Finally, we conducted stepwise multiple logistic regression analysis in which above significant variables were used as independent variables. Number of subjects entered into the stepwise multiple logistic regression model were 4438 in group II and 3483 in group I. Entered variables were age, gender, BMI, family history of cancer, smoking, alcohol consumption, total daily calorie intake, folate intake, salt intake, dietary habit (out-eating, overeating, irregular eating), and *H. pylori* seropositivity.

Old age ( $P = 0.000$ ), male gender ( $P = 0.000$ ), *H. pylori* seropositivity ( $P = 0.010$ ) and current smoker ( $P = 0.000$ ) were significantly more common in the group II at multiple logistic regression model.

## DISCUSSION

Gastric cancer was recognized as the first leading cause of

cancer death in Korea<sup>[1]</sup> and many epidemiologic studies about risk factors for gastric cancer were reported<sup>[5,6]</sup>. So far, we had no a large-scale epidemiologic studies about metaplastic gastritis, precursors of gastric cancer in the Korean population.

In the early 1970s, Correa formulated a multi-step model of gastric cancer, which postulated a sequence from chronic atrophic gastritis, intestinal metaplasia, dysplasia and gastric cancer<sup>[2]</sup>. Chronic gastric inflammation leads to repetitive injury and repair resulting in hyperplasia<sup>[3]</sup>. Whereas acute injury and inflammation associated with healing are usually self-limited, chronic injury or inflammation leads to a sustained expansion of tissue proliferation<sup>[7-10]</sup>. Sustained tissue proliferation is generally accepted as a risk factor for cancer<sup>[3]</sup>. As is well known, metaplastic gastritis is precursors of gastric cancer.

Our understanding of gastritis and cancer underwent a marked shift with rediscovery of *H pylori*<sup>[7-13]</sup>. *H pylori* is now thought to account for most of gastritis<sup>[13]</sup> whereas *H pylori* infection is not an only important factor for development for gastric cancer<sup>[5]</sup>. But, it is not clear whether *H pylori* infection is also important for development for metaplastic gastritis. Our study demonstrated that *H pylori* seropositivity is an independent risk factor for the metaplastic gastritis.

In the intestinal type of gastric cancer, environmental factors other than *H pylori* infection seem to play a part in the carcinogenesis<sup>[12]</sup>. Environmental factors may facilitate the development of atrophic gastritis and intestinal metaplasia<sup>[12,14]</sup>. Based on epidemiologic studies of dietary histories, the first step in the Correa pathway was believed to be initiated by a diet rich in salt and nitrates/nitrites as well as deficiencies in fresh fruits and vegetables<sup>[5]</sup>. Dietary factors and continued effects of chronic inflammation were felt to be responsible for the progression from gastritis to atrophy, metaplasia, dysplasia and carcinoma<sup>[12]</sup>. Ingestion of sodium chloride is thought to promote gastric carcinogenesis<sup>[14]</sup>. Exposure to N-nitroso compounds probably facilitates advancement of chronic atrophic gastritis and intestinal metaplasia in adulthood<sup>[5]</sup>. Our study showed that neither dietary habits, salts nor folate intakes is a risk factor for the metaplastic gastritis. The major limitation of our study is that diet survey used in our study is carried out by not-validated questionnaire.

Both superficial and chronic atrophic gastritis are common in alcoholics<sup>[6]</sup>. Alcohol consumption can also cause acute gastritis<sup>[15]</sup>. Our study demonstrated that alcohol is not a risk factor for the metaplastic gastritis. Male dominance of the metaplastic gastritis can be explained, in which male gender tends to have more dangerous environmental factors such as smoking. But, our study demonstrated that male gender and smoking are independent risk factors for the metaplastic gastritis, respectively.

First, the limitation of present study is selection-bias. The substantial numbers of subjects did not have information about all items of the questionnaire. Numbers of subjects entered into the multiple logistic regression model were 4438 (4438/13578, 32%) in group II and 3483 (3483/10521, 33%) in group I. The other limitation of our study is inter-examiner or intra-examiner bias

**Table 2** Multiple logistic regression analysis about risk factors for development of metaplastic gastritis

Variable <sup>1</sup>	Odds ratio (95% CI <sup>2</sup> )	P value
Age	8.945 (7.204-11.105)	0.000
Male gender	1.144 (1.133-1.155)	0.000
Current smoking	2.137 (1.693-2.697)	0.000
<i>H pylori</i> <sup>3</sup> seropositivity	1.223 (1.049-1.426)	0.010

<sup>1</sup>All variables in the model are as follows: age, sex, body mass index, family history of cancer, smoking, alcohol consumption, total daily calorie intake, folate intake, salt intake, dietary habit (out-eating, overeating, irregular eating), and *H pylori* seropositivity.

<sup>2</sup>CI, confidence interval.

<sup>3</sup>*Helicobacter pylori* is abbreviated as *H pylori*.

of endoscopic diagnosis about metaplastic gastritis and normal. To ascertain the precision in endoscopic diagnosis of gastritis, we undertook a pilot study on 10 individuals. Endoscopic finding was obtained 2 times on 10 individuals by 2 examiners. We examined the inter-examiner bias between 2 examiners and intra-examiner bias between 2 examinations by same examiner. Kappa value of intra-examiner was 1.0 ( $P=0.002$ ), 0.737 ( $P=0.016$ ), respectively. Kappa value of inter-examiner was 0.875 ( $P<0.001$ ).

Our data suggested that old age, male gender, *H pylori* seropositivity and smoking were risk factors for metaplastic gastritis, precancerous lesion of gastric cancer.

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